UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF WEST VIRGINIA

Biogen International GMBH
and Biogen MA, Inc.,

Plaintiffs,

vs. CIVIL ACTION NO.

1:17-cv-116

Mylan Pharmaceuticals, Inc.,
Defendant.

VOLUME II

- - -

TRANSCRIPT

of proceedings had in the bench trial of the above-styled action on February 6, 2020, before Honorable Irene M. Keeley, District Judge, at Clarksburg, West Virginia.

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Thursday Morning Session,

February 6, 2020, 10:43 a.m.

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(In chambers.)

THE COURT: This is -- I'm going to call this a bench conference in Biogen versus Mylan, 1:17-116. And will counsel who will be handling the motion and the report today please note their appearance, beginning with Biogen.

MR. BROWNING: Paul Browning, counsel for Biogen.

THE COURT: Okay.

MS. BLOODWORTH: Shannon Bloodworth, counsel for Mylan.

THE COURT: Okay. All right. So it looks like you're going to lead on this, Ms. Bloodworth, if you want to.

MS. BLOODWORTH: Sure. Thank you, Your Honor. So obviously, thank you for the time and the consideration of having us here today. We have gone through and removed two of the fact witnesses who were designated to participate in this case. We have obviously removed all of our 103 arguments from the case, and I also have reviewed the remaining fact witness dep designations to confirm they are only relevant to 112.

I still have a final review of one additional fact witness by dep designation that I think there is some additional information we can cut, and so I've proposed to Biogen that we would give all of our dep designations final over to Biogen by 9:00 p.m. tonight, including the dep designations that we will

be providing for Drs. O'Neill and Dr. Katherine Dawson, who were going to appear at trial and now are -- were witnesses on our "may call" list and now we are going to be using their testimony adversely affirmatively in our 112 case.

THE COURT: They're by video.

MS. BLOODWORTH: They'll be by video.

THE COURT: And designation.

MS. BLOODWORTH: And designation.

Your Honor, there's a lot of testimony by specifically Dr. O'Neill, but we're going to try to slim down any redundancies and make the video dep designations the primary reference point so that we can have it efficient and also have it in the best medium for the Court to see the witnesses.

And so I think what we were hoping to do was play those dep designations starting with the inventor, Lukashev, today at 1:00. I believe we're set to go with those.

MR. BROWNING: Yes.

MS. BLOODWORTH: And then we were going to follow that and finish out the day with deposition designations from Bozic and Sibold. And I believe the parties have agreed on the content of those dep designations. I have not seen the motion that was just filed, but it's my understanding that it's a motion to strike those witnesses from being in the case due to relevancy.

And so setting aside that issue, just to finish out the procedure for the rest of the time, we will call Dr. Greenberg

tomorrow morning, live. And he will testify on 112. Dr. Wynn, their expert, will then follow Dr. Greenberg, and then again pending, I think, the dispute in the motion and our cutting down Lansden's dep transcript, we think we could finish the day with that dep video testimony and have a full court day tomorrow.

THE COURT: Okay. And then how about the next week?

MS. BLOODWORTH: And then we would start with Dr. O'Neill on Monday morning, and then also Dr. Dawson again, pending the outcome of this motion. I think she's also involved in it, based on the little I heard this morning about this issue.

And then, Your Honor, because we haven't done those designations yet, although the parties have agreed on a procedure for getting those accomplished, I don't know exactly how long they'll take on Monday. It could be a substantial amount of the court day. And so I think it would be the Court's preference for us to start closings right away, but potentially have to split them up or just start closings on Tuesday morning.

THE COURT: I think it makes more sense, if you all don't mind being here, to start them on Tuesday morning to give you a chance to clean things up and organize it.

MS. BLOODWORTH: Great.

THE COURT: That way you can stay up all Monday night.

MS. BLOODWORTH: You understand too well.

So we will have that procedure. And I think procedurally we're in accord on that general --

MR. BROWNING: It's the substance we disagree on.

MS. BLOODWORTH: It's the substance we disagree on. And again, I haven't read this, Your Honor, but understanding the timing and the Court's timing, I'm happy to address any issues about these witnesses' testimony, if they want to raise them now.

THE COURT: Okay. Do you want to be heard on this right now? I will be candid. I have not had time to look at this.

MR. BROWNING: I understand.

THE COURT: Just literally hot off the press.

MR. BROWNING: Your Honor, and I apologize for that. Ordinarily we would never do that to you, but this -- obviously, the case has changed dramatically since yesterday, and this is an entirely new theory that was sprung on us Monday night, so we're in a position where we have been scrambling as well, so that's why it's just coming before the Court right now. So I'm happy to do it right now, or whatever Your Honor would prefer.

THE COURT: My recommendation would be give me till 11:30 to take a look at it. That will give you an opportunity as well, and come back in here -- I know Judge Kleeh is in the courtroom right now, and he's expected to stay in there, right?

THE CLERK: His next hearing, I believe, is at noon.

THE COURT: So he has a noon hearing. So we'll come back in here and I'll hear the argument then and hopefully I'll have digested what the issues are and I would hope to be able to make a ruling when you're finished with your arguments.

MR. BROWNING: Thank you, Your Honor.

THE COURT: That will allow us then -- I will give you time to get back down to the courtroom, and if we have to start at 1:30 instead of 1:00, that's fine. We'll just do whatever we have to.

Also, it looks now like -- I don't know how far into next week -- you think it will go Tuesday, is what it sounds like. We could do it up here, because Judge Kleeh is going to be in trial now in Elkins, another courthouse we have, which means that the work that was going to be in this courthouse -- in this room is cleared off now, so I can have it back. And I think for the last couple of days that might be a lot more convenient for you, since you're going to be -- you're not going to be working in the courthouse over the weekend, so moving in here on Monday wouldn't be too inconvenient, if you wouldn't mind.

MR. BROWNING: That's fine.

MS. BLOODWORTH: No.

THE COURT: I think you'll appreciate it. I know I will.

Okay. Let me have a little bit of time to take a look at this and to try to reference it to exhibits that I'm sure are

mentioned in here.

MR. BROWNING: Your Honor, I'll just explain the parameter of the dispute. I'm not going to argue it, obviously, but we did meet and confer this morning, and while we don't agree about the relevance of Dr. O'Neill and Dr. Lukashev, we haven't contested them in this motion. It really is just about Lansden, Bozic, Sibold. I believe those are the -- and Dawson. Excuse me.

THE COURT: Okay. Just haven't looked at anything. But just so you know -- you've heard me say this before -- this is a trial to the bench. I have a lot of discretion to determine what weight I will give to anything, whether I'm going to consider it at all, and as long as I let you know that in my opinion, it should be satisfactory.

My inclination in a trial like this is always just let it all come in and I'll figure it out. But I understand you need to make this argument. Okay? All right. Thank you.

MS. BLOODWORTH: Thank you.

(Recess taken, 10:52 a.m.)

(In chambers at 11:48.)

THE COURT: Ms. Bloodworth, as we get into this, could I just ask you, do you remember the date on which Mylan filed document 352, which is your second amended invalidity contention? Do you know the date?

THE LAW CLERK: September 28, 2019.

THE COURT: September 28. Okay.

MS. BLOODWORTH: I do too. Thank you, Your Honor.

THE COURT: This is Biogen's motion.

MR. BROWNING: Thank you, Your Honor. I'll be brief. I know Your Honor has just read the papers. Our position is we have -- there are two reasons why we're moving to exclude the evidence at issue. And that's because it's completely irrelevant.

THE COURT: I just want to make sure that I understand what you're seeking to exclude: Sibold, Lansden, Bozic, and Dawson.

MR. BROWNING: Correct, Your Honor.

THE COURT: All or some.

MR. BROWNING: All. We do not think there's anything in the testimony that is relevant to the 112 issues.

THE COURT: You have me at a disadvantage. I don't have that testimony in front of me. So I'll take as a basic understanding here that all of this testimony relates solely to 112 issues.

MR. BROWNING: No. Our position is exactly the opposite. It does not relate to 112 issues at all. I'm not sure what it related to, perhaps obviousness, perhaps other issues, but it did not relate to 112, in our view. I'll try and give you some flavor. It involves research and development efforts, confidential at Biogen.

THE COURT: But I guess I didn't phrase that very well. Your arguments arising under 112.

MR. BROWNING: Yes. I'm sorry, Your Honor. Yes. Let me rewind and I'll try to make myself clear.

THE COURT: I understand that you don't think it comes in, believe me, I understand that, but is all arising under 112 and only 112.

MR. BROWNING: Correct. Our argument is it's not relevant to the remaining issues in the case, which are limited to 112.

THE COURT: Then for my purposes we'll start with what 112 is all about.

MR. BROWNING: Correct. 112 is, the statute makes clear, you look at the four corners of the patent specification viewed from the perspective of a person of ordinary skill in the art, and that applies both to written description and enablement. And that's the fundamental problem we have here is the type of evidence they're seeking to rely on is internal confidential information that has no bearing on how a person of ordinary skill in the art would view the patent specification.

And I think that point is particularly highlighted by the Allergan case we cited, which I know Your Honor has seen, and in that case the CAFC found it was legal error to look to internal undisclosed protocols, is the way it's described in the case, that related to FDA submissions.

We have the precise issue here. Some of the testimony that

you may ultimately hear relates to the details of FDA protocols, so we're dealing with a precise type of information that the federal circuit has found to be irrelevant to the analysis.

And if I could, maybe I can elaborate a little bit. We did meet and confer this morning because I wanted to -- because Your Honor directed us to, obviously, but to get opposing counsel's perspective as to why they believe this evidence is relevant. And Ms. Bloodworth, I'm sure, will have more to say, but two things stood out to me. One is that it was allegedly circumstantial evidence in support of their theory that there's a lack of written description support. We disagree that this is any valid circumstantial evidence, because it doesn't relate to what a POSA would think. This is about what business people at Biogen may have thought. They're not persons of ordinary skill. Even any skilled individuals at Biogen are not a person of ordinary skill, because they're privy to Biogen's information. So it's completely irrelevant and prejudicial --

THE COURT: The people who are at issue here, or the testimony that's at issue, has to do with commercial success, so it wouldn't be a POSA.

MR. BROWNING: Right. That's my point. It's business-type information. They're people who aren't scientists.

THE COURT: Would it come in under 404(b)?

MR. BROWNING: Your Honor, I'm sorry. I don't have the statute in front of me.

THE COURT: That's the criminal -- usually used in criminal evidentiary rules, but other evidence not being admitted -- not ordinarily admitted but coming in because it may support a motive or it may support some other admissible reason why it can come in, even though it's not the usual type of evidence that would support the claim in chief.

So I looked at this and thought from the opening statement, well, is this coming in to basically show that it was the FDA who suggested the dosage of 480 milligrams, because commercial people were saying no, we want the higher one because it's more commercially viable to us in terms of kind of success, financial success, we'll have.

And I looked at it -- I have no idea if that's why they thought it would come in, but that is what I thought, is this coming in as like a background information to help me understand why, as they argued, there's only one mention of 480 in the written description.

MR. BROWNING: That may be an accurate description of their theory. I don't really know. But Your Honor, that's exactly why it's irrelevant and prejudicial. The motivations --

THE COURT: That would be a 403 argument, and I understand that. But you're basically saying it doesn't come in under any

rule of evidence.

MR. BROWNING: Correct, Your Honor. Because we -- again, the federal circuit has found it's legal error to rely on this type of information. We do not think it should be in the record. And really we're looking at what one of ordinary skill in the art would understand based on what's in the patent specification.

And I think it's also important to point out, Your Honor, that also in opening statement counsel were candid in explaining that they don't contest that Dr. O'Neill conceived the dose of 480 milligrams per day. So any arguments that others of the company didn't agree with Dr. O'Neill are really irrelevant, twofold. First of all, it doesn't matter what someone internally at the company thought to how a POSA would view the specification. Moreover, if Dr. O'Neill truly believed in this invention and conceived of it, which has been conceded, I believe, then if others didn't, it doesn't bear on the issue.

THE COURT: Does this information go to prosecution history?

MR. BROWNING: I'm not sure exactly what Your Honor is asking. This information is not in the prosecution history, as far as I know, because it's confidential internal business information that's never there.

But that does lead me to the second point, if I may, Your

Honor. The other argument that was discussed this morning in our meet and confer relates to Dr. Dawson's testimony, who did submit a declaration during the prosecution history. But here that related to obviousness. And we're very concerned there's an effort to conflate the issues of obviousness and written description, and they're completely different issues. One is what one of --

THE COURT: That doesn't mean the same evidence can't be used to support either argument, both arguments.

MR. BROWNING: That may be true, Your Honor, but here is a declaration about the specific issue of what one would understand without the patent. That doesn't bear on what someone would understand with the patent.

THE COURT: Okay.

MR. BROWNING: So we believe that's completely improper and unfairly prejudicial to us.

THE COURT: Okay. Now, I understand the impropriety argument. I understand that if it is improper, it would be prejudicial. When I read over the brief -- and it was obviously very quickly -- there was a lot of argument about -- I thought, about surprise and that kind of thing, which I thought may have overstated the issue here, since -- I get that you may not think this should come in, but that there's only one mention, if that is true, I was going through to find out, of 480 milligrams in the patent, that's not surprise to you.

You know better than anybody what's in your patent. So this isn't what I would call the classical, we never heard this before, we didn't know any of this. This is more in the line of, we didn't expect this argument to come up on this issue. It's not that we're not aware of these facts. We know what Dr. Dawson said. After all, she's our witness and all of that. Could you clarify for me how you really intend me to look at this argument.

MR. BROWNING: In all fairness, Your Honor, I think that's mostly a characterization we would agree with, in that certainly we're aware of the facts that these are deposition designations that have been out there. The problem is that they were never identified as part of the 112 defense, and therefore we didn't have the opportunity to move to exclude them earlier --

THE COURT: Yeah, but you have the opportunity now. You have the opportunity, indeed, after the trial is concluded, to argue that they're irrelevant, immaterial, prejudicial, under 403, if that's where you mean the prejudice to lie, and I'm trying to understand, since the facts themselves don't surprise you, why wouldn't I just hear it out and decide whether, under very clear rules about what I can consider under 112, that whether they're in or out.

MR. BROWNING: Right. Your Honor, with all due respect, the disclosure rules are there for a reason, and there are

multiple disclosure rules that have been disregarded here.

THE COURT: You think it's the theory of the case disclosure that's the prejudice here. You should be aware of that.

MR. BROWNING: Exactly, Your Honor. I can see that the facts -- obviously, we know about the deposition transcripts and they didn't come out of the blue. And I can't argue that with any credibility. But the problem here is we never knew this would be a 112 argument. And if it had been, we might have made different decisions with our expert reports --

THE COURT: Wouldn't a good trial lawyer consider all possibilities? I mean, I don't think you're going to sit here and say, we didn't look at this as a possibility, but gee whiz, they didn't designate it so we don't have to prepare for it. Isn't the real prejudice to you all there?

MR. BROWNING: Your Honor, with respect, I disagree. We try our best --

THE COURT: You hadn't conceived they would argue this.

MR. BROWNING: No, we did not. It's generally a surprise. It's not a relevant argument.

Now, to be clear, to be candid, this does sort of sound like certain arguments that were raised in Delaware, so I'm not going to say this is completely coming out of left field, but we didn't anticipate it in this case, which is important, because in Delaware we had the ability to have our expert

reports crafted to respond to this argument. Here we didn't have that ability. So we've got a real problem with not being able to expand our expert testimony to cover a new argument in 112, and that prejudices us in a significant way.

Moreover, the evidence we put in was developed differently because the issue was never raised, so while this is not a theory that I've never heard before -- I can't say that -- it's certainly a theory we're not prepared to try in this trial, and that's a problem for us.

THE COURT: Okay.

MS. BLOODWORTH: Thank you, Your Honor. May I go? Okay.

So first off, I'll start where Your Honor did, on the legal issues and the paradigm here that they are looking and why we think this is relevant to 112 and our written description defense.

The federal circuit has been very clear in the Synthes v. Spinal Kinetics case, as well as in the Nuvo v. Dr. Reddy case, that an inventor's testimony, as well as noninventor testimony, such as employees who are, for example, the manager -- research and development manager, are able to shed light on -- are allowed to illuminate the lack of the disclosure in the specification in a 112 context.

And so what I was -- what I think is very clear is that you can't, under the 112 context, have inventor testimony fill in a hole in a patent specification. You can use extraneous

evidence, including internal documents, to shed light on why there was not a disclosure in the first place.

And again, we have a burden by clear and convincing evidence, and it's a fact question, and we agree that the standard is reading the patent specification in light of the prior art as a skilled artisan, but we also get to put on evidence for why it would be, and that's what you heard --

THE COURT: Why it would be what?

MS. BLOODWORTH: Why that element may be missing.

THE COURT: Okay.

MS. BLOODWORTH: Right? It's not that -- again, it goes to almost the credibility of the argument, and I think that's how it's been used, circumstances internally that people would know X, Y or Z. And the federal circuit has clearly held that's a viable reason for this evidence and that's what we're submitting it for.

And in the opening argument we said in the slide, it said lack of written description, they didn't attach it to their motion. It was slide 35, right before -- if you look at Exhibit A, they attach slides 38, 39, and again, this is deposition testimony cited from the witnesses we're talking about, Lansden, and I believe --

THE COURT: I think the point, if I understand their point, is, yeah, okay, that's all there, but it doesn't matter, can't come in.

MS. BLOODWORTH: And I would say, Your Honor, I think the federal circuit has said otherwise. And if I can read --

THE COURT: The Dr. Reddy case?

MS. BLOODWORTH: It's the Dr. Reddy's case, Your Honor, and I have a copy of it, I think.

THE COURT: My legal file is down at the other courthouse.

MS. BLOODWORTH: It's the Nuvo case, Your Honor, versus Dr. Reddy. And if you look on page 11, and that is 923 F.3d 1368 (2019) from the federal circuit. And the last sentence before Section C says, although inventor testimony cannot establish written description support where none exists in the four corners of the specification, it illuminates the absence of critical description in this case.

And in this case, the federal circuit relied on the inventor's testimony for saying things such as, I only hoped it would work, I didn't know it would work, maybe thought so. And it's very clear you can't get a patent claim with a valid specification on a wish or a hope. And so that's directly relevant. So we have the inventor testimony. They dropped that objection, is my understanding. But the proposition isn't so narrow.

And we turn to the Synthes case I mentioned earlier. It takes a little more explanation, but again, the reporter cite is, 734 F.3d 1332 (2013) from the federal circuit. And if you could turn, please, Your Honor, to page 7, we'll see a

discussion in the second full paragraph that starts, SK presented testimony regarding the plurality of openings limitation via their expert, Dr. Lee, and its research development manager, Mr. Koske.

So Mr. Koske in this case is a fact witness internal to the party. And again, the Court went on, the bottom of page 7 to the top, 1342 to 1343, to talk about Mr. Koske's testimony, how it relied on internal information, months of work, what it meant.

And if you get to the bottom of the first column on the left-hand page of page 8, the Court concludes and says, taken together, Mr. Koske's testimony is at least circumstantial evidence that it would not be evident that peripheral grooves on the cover plates would disclose to skilled artisans that internal slots would serve the same function. Mr. Koske's testimony and exhibits used during it, coupled with Dr. Lee's testimony, provided ample evidence for the jury to conclude the written description did not support the broad claim limitations in the asserted claims.

And so, again, it's far from clear that the only evidence a court looks to is the skilled artisan. And that is, I think, the fundamental disagreement between the parties. We think it goes to weight, not to a bar of relevance. We do think it goes to -- a lot of this testimony will go to motive and to the selection of not including the information in the patent

specification.

THE COURT: Which I consider, what I said, earlier 404(b). Well, let me ask this question: At the time of the final pretrial conference, what did you understand Mylan's theory of the case under Section 112 issues to be?

MS. BLOODWORTH: Your Honor, this is what we understood. Our pretrial order does only lay out the legal requirements on all of our issues. We were consistent with that.

THE COURT: This is 352, your second amended -- no. That's earlier. Why don't you start there. That's August 28th of 2019, and then we have the section from the -- did you all submit the section from the final pretrial order?

MR. BROWNING: I'm sorry.

THE COURT: Did Biogen submit --

MR. BROWNING: Yes. It's Exhibit 14, I believe.

THE COURT: Is that D? Your Exhibit D to your motion.

MR. BROWNING: I think it's C and D, I believe. Yes, I believe it's C and D.

THE COURT: So Exhibit 14, under which is Exhibit D to your motion, states, defendant's brief summary of the material facts and theories of liability -- would that be the first place to look?

MS. BLOODWORTH: That would, I think, Your Honor, be the first place to look. However, I will be candid and tell you that that's not going to lay out the factual underpinnings --

THE COURT: I'm trying to see the evolution of the arguments.

MS. BLOODWORTH: So the evolution of the argument, Your Honor, is, as you know, we coordinated our fact discovery very closely with the Delaware defendants in the Delaware case. We were taking depositions months after the close of fact discovery in our case, to only do them once in both cases, and the Delaware case was significantly behind ours.

And so we have developed these cases pretty closely in tandem, and all of this information -- I don't have the contentions I'm going to take for face value that it's not disclosed in there in this way, but it was certainly tried in the Delaware case and what it is is all the same factual information.

THE COURT: I will disclose there were a couple of highlights here, but I have the contentions with regard to written description --

MR. BROWNING: I don't mind at all.

THE COURT: I didn't write on it.

MS. BLOODWORTH: This is the seconded amended?

THE COURT: Filed in August.

MS. BLOODWORTH: Yeah. And so, again, it's the law on the issue, fails to provide a skilled artisan. If anything, it points to skilled artisan -- it points a skilled artisan to about 720 as that dose is called out with specificity and is

the only dose that is being administered in two or three, four, or six separate doses. That's the argument about the fact that 480 milligrams only appears once in the patent.

So we disclosed in this case certainly on the -- when we provided our opening slides on Monday at noon, we definitely put in all the same evidence as the Delaware case, and did so under the heading of written description, again, everything that -- I think it's almost the same in both cases that was tried in the Delaware case in December. And we put it in and didn't receive any objections, and we put in our dep designations on Monday night on this very issue and why it would support 112, and we got their counter-designations on Tuesday night and we had a meet and confer on Wednesday morning and no objection was raised at that time. And it was very clear that this was our story under 112, as they said it was in our opening argument. It was put in under 112, it goes to the reason of the lack of disclosure in the patent application, because after the defined studies were revealed, it was then and only then that they went back in time to amend the patent specification.

And then, Your Honor, just on one other point on the Dawson testimony, which is different. Dr. Dawson has submitted several declarations and has testimony about the fact that the skilled artisan would think that the 480 milligram working was unexpected. And that goes directly to the heart of what is the

mind set of the skilled artisan reading the patent specification. And it was submitted both in the patent office and they called her in Delaware and we deposed her on that very issue. She was a key witness to Biogen on unexpected results.

And of course, it's not only a party admission that the skilled artisan would not expect 480 milligrams to work. When the declaration was filed as a part of the file history, it's a binding admission of the state of the art at the time.

So Dr. Dawson's declaration and statements on that unexpected results was included in Dr. Greenberg's opening expert report and cited for that proposition in his 112 section.

So they have been aware that we were going to rely on nonskilled artisan internal evidence as least as long ago for Dr. Dawson as Dr. Greenberg's opening expert report. And we never heard any objection to that until this morning.

THE COURT: All right. Now, just help me work through this, because as the judge I always go back to the beginning, the patent. So with regard to what Mylan is picking apart in its case, the mention of 480 milligrams per day obviously comes up under the claims.

MS. BLOODWORTH: Yes, Your Honor.

THE COURT: And claim one thereof is about 480 milligrams per day and prior to that it comes up.

MS. BLOODWORTH: It's column 15, Your Honor.

THE COURT: That's right. Okay. Not 18. 15. Actually, I don't have any 15.

MR. BROWNING: I think it is column 18.

THE COURT: That's what I thought. So it comes up in the beginning at line 58 and column 18: For example, an effective dose of DMF or MMR to be administered to a subject orally can be from about 0.1 grams to 1 gram per day, 200 milligrams to about 800 milligrams per day, e.g., from about 240 milligrams to about 720 milligrams per day, or from about 480 milligrams to about 720 milligrams per day, or about 720 milligrams per day. And then it goes on to give the example of how you would dose the 720 milligrams per day in separate administrations of two, three, four, or six equal doses.

So when you are going to ask me to look at the written description, what parts of the patent are you going to direct me to?

MS. BLOODWORTH: Sure, Your Honor. We are going to direct you to -- first of all, we'll have Dr. Greenberg explain all the specification as a skilled artisan would understand it, and 480 milligrams is only mentioned on column 18, as Your Honor noted. So the issue is does a skilled artisan reading the specification believe that 480 milligrams of DMF would work to treat MS.

And the clear history of this case is that Biogen has taken the very strong position that no skilled artisan would think

480 milligrams would work until in 2011, years after the patent specification was published. Only then were skilled artisans surprised and thought that it would work. And that is why we rely upon Dr. Dawson's testimony, who said that in also the patent office to get the patent allowed, and it's the viewpoint of the skilled artisan.

So if a skilled artisan, thinking that the patent would not work, reads the patent specification and doesn't see why it would work, the issue of whether or not 480 milligrams can be administered as a tablet isn't the issue. That's not the claim. The claim is that it has to be therapeutically effective to treat MS, and that's the exact holding in the Nuvo v. Dr. Reddy case where the district court found that the specification was specific.

THE COURT: Let me go back. This is a patent for the treatment of multiple sclerosis. And it's a continuation and the filing date here is February 13th, 2012. And do I take from that that it was after 2011 that the patent was -- what happened? What happened? I'll get to the bottom line. Was 480 milligrams mentioned as of what's the date?

MS. BLOODWORTH: February 8, 2007. Yes, Your Honor, 480 milligrams was in the -- it was mentioned in the publication of that application in 2008.

THE COURT: So if it was mentioned, as it is here, in the -- as of August 12th -- August 2nd, 2012, you're wanting

this information to come in to show that they didn't have that understanding, no POSA would have that understanding in 2007. But wouldn't that put me in a position where I was looking at something outside of the patent that I'm not supposed to look at to determine the 112 issues?

MS. BLOODWORTH: Your Honor, you are allowed --

THE COURT: You're wanting it in for the truth of the matter asserted, and you're wanting it in for me to reach a conclusion that Dr. Greenberg's testimony is true with regard to, in 2007, assuming he's going to say this, no POSA would have understood that 480 worked. And here are the statements of Biogen that confirm nobody knew that, but it was in the patent.

MS. BLOODWORTH: It's not in the patent that it would work. All the disclosure in the patent is that you can have a composition of 480 milligrams. A skilled artisan reading that --

THE COURT: A method of treating a subject, et cetera, consisting essentially of, A, a therapeutically effective amount of DMF or MMF, or a combination thereof, and the excipients isn't the issue, or a combination thereof is about 480 milligrams a day.

So if I read that, as I think I'm supposed to read it, they're claiming a therapeutically effective amount of DMF that is about 480 milligrams per day. And I was curious, is that in

the 2007 submission, and it is.

MS. BLOODWORTH: It is, Your Honor. And this is exactly what happened in the Nuvo case. The district court saw in the specification that there was a disclosure of the amount of the dosage and the use and said, oh, it's sufficient. But in the obviousness case, plaintiffs had also made the argument that a skilled artisan at that time, reading that patent specification --

THE COURT: We don't have an obviousness case now.

MS. BLOODWORTH: Right, but we still have all the testimony and we have their admissions in the patent prosecution history, which are binding.

THE COURT: Why would it be relevant on the 112 issue?

MS. BLOODWORTH: That's what I'm going to get to, Your Honor, because the patent doesn't say why it would. The patent doesn't add anything to the art. And in fact, the testimony will say, even reading the patent specification, nobody thought it would work. And that's what the Nuvo court, the federal circuit, reversed the district court on that very finding and said, you have to put something in your specification to hook and explain and move the art forward to why a skilled artisan, thinking it's not going to work, would read your patent specification and change their mind.

And this patent specification, you'll hear from Dr. Greenberg, has nothing in it, preliminary data, prophetic

example, you know, anything, that would tell a skilled artisan, oh, that might work.

THE COURT: I will say that I went diving into the examples thinking there will be an example of that dosing there. There isn't.

MR. BROWNING: No, Your Honor. It's not required. And I obviously disagree with Ms. Bloodworth's take on the case law. The patent discloses 480, as Your Honor has observed, and that was in the original priority submission in 2007, and it actually says specifically it will work. It's effective. It makes the statement, when administered orally at that dose, and that's sufficient. It discloses the claimed invention. This is about disclosure, not --

THE COURT: You're talking about lines 58 through 64.

MR. BROWNING: I believe I am. Column 18, correct, Your Honor.

And what Ms. Bloodworth is referring to, the Nuvo case is a very unusual case. There the patent specification said people don't think this will work. It's a very unusual specification. Typically wouldn't make that kind of comment. We certainly don't. But the specification said the POSA would not think this would work, and then never says why the inventor does.

Here we have the opposite situation. Here our inventor says these doses are effective. So under the case law, that's sufficient. The federal circuit is very clear, even in Nuvo,

you don't need examples, you don't need test data. What you need is a disclosure. Here the invention is treating patients with multiple sclerosis with a specific dose. And that's clearly described.

THE COURT: Now, let me ask this: Does Biogen have any objection to the testimony of Dr. Greenberg from his own experience, training, as a POSA?

MR. BROWNING: No, Your Honor. And to be clear, we think that it's fine for a POSA to acknowledge what they know. And so the inquiry is to the four corners of the patent, but it's not somebody who knows nothing. It's a POSA.

THE COURT: Are you calling a POSA on this issue? I know what POSA is. Are you calling your own?

MR. BROWNING: Dr. Wynn.

THE COURT: So will Dr. Wynn be testifying that as of the submission of the patent or the filing of the patent in 2007, no POSA would have expected this dosing to work?

MR. BROWNING: That would have been his --

THE COURT: That would have been his obviousness --

MR. BROWNING: -- his obviousness testimony.

THE COURT: What's on the 112 issues?

MR. BROWNING: Here we have a patent specification disclosing the invention, so if the standard were that anything surprising wasn't patentable, then we'd have no patents. You need to have an advance that is not obvious over the prior art.

THE COURT: So it has to be understandable to the POSA.

MR. BROWNING: Disclosed, it needs to be disclosed.

THE COURT: It has to be more than that. It has to be understandable to the POSA.

MR. BROWNING: Right.

THE COURT: And show that the inventor actually invented the invention claimed. That's our area and everybody is relying on that. And under enablement, whether the POSA, after reading the specification, would be able to make and use the clinical invention without undue experimentation, let me just move to that issue. This is just dosage. So we're not into the usual -- what I would say, my experience, limited though it may be, is the more usual enablement arguments. What's your argument there?

MS. BLOODWORTH: So Your Honor, if I may, there is -- certainly that is the requirement to disclose and make and use the invention. The Nuvo case actually says that's not enough. You need to do more than that for written description.

THE COURT: That's what Allergan says, that you just have to be able to make and use the claimed invention.

MS. BLOODWORTH: Reading from the Nuvo case, Your Honor, at part -- page 1382, it says, teaching how to make and use an invention does not necessarily satisfy the written description requirement.

THE COURT: But I was just asking about enablement.

MS. BLOODWORTH: So the enablement argument is largely based on the written description argument.

THE COURT: They're going to basically conflate.

MS. BLOODWORTH: They're going to conflate. We'll obviously brief them separately under the law. It's the same set of facts. And the reason why, frankly, we put in the facts on both is because oftentimes written description and enablement get confused, and this is a case where even if you find that you can make and use the invention, you still don't satisfy written description for why a skilled artisan would think it would work.

THE COURT: Okay. I don't think I need to give you this ruling before this afternoon's testimony. I'd like to have a little bit of time to mull it over, basically because if I were -- if this were an ordinary case, I would let this in. I don't find the prejudice to Biogen so overwhelming that it wouldn't come in, because I think the concept of all of this was well understood by Biogen, or the target, if you will, of Mylan's argument was understood.

This is an issue as to whether these particular witnesses can offer relevant testimony in support of their theory of the case. Okay? And I understand that. And I also understand that in a patent case, the art of making these decisions under what are the ordinary rules of evidence is sometimes different. And I do know that I have to limit my understanding of the

testimony to the four corners of the specification and I should not go outside it, right?

MS. BLOODWORTH: We would disagree with that proposition.

THE COURT: I know you disagree, but that's been drilled into me over time, so I'm going to have to look at this Nuvo case, and I also want updated and make sure that -- it's 2019. Has anybody else written on this subject since Nuvo?

MR. BROWNING: That's a good question, Your Honor. I'm not sure.

MS. BLOODWORTH: Not that stands out.

THE COURT: This is Judge Clevinger with Judge Prost and Judge Wallach, and I think it's important for me as a district judge to respect that the federal circuit -- that I need to read broadly on this topic within the scope of the circuit's more recent decisions rather than read this case in isolation, in order to understand whether there's a broader understanding within the federal circuit now as to how to take some of this fact evidence and how to weigh it.

So let me do that. We need to get on with what we're doing today. And I know you need the ruling today and you'll get it today. But I need to look at this a little bit more carefully. My inclination, however, at this point is, again, I know how to weigh evidence and if I -- I'd rather -- from an appellate perspective, I, as a district court, would rather let this in and I can discount it after I hear it and say that really is

irrelevant and it's not material to this case and I'm not going to rely on it; even though it comes in, it's not being relied on. That way I don't have -- and you don't have an appellate court saying, should have heard that. Better to hear it and not rely on it than not to have heard it at all and have an appellate court say, you should have taken a look at that and then as much as I like all of you, you're back before me.

So you all are -- I don't know how many of you are old enough to remember the days when the federal circuit affirmed in part, vacated and denied -- I mean, as district judges we used to say to the federal circuit, please don't do that to us. Either just tell us it's all back or make the decision yourself.

So in other words, that's where I'm leaning. But I understand that you need a record and I will give you my most articulate reasoning as I finally decide what it is at the end of today. Okay?

MS. BLOODWORTH: Thank you, Your Honor. May I make one more request, since, again, I'm a little on the fly here this morning on this issue.

THE COURT: You would like to brief it.

MS. BLOODWORTH: I would like to put in a posttrial brief. We have dep designations for tonight, for today. We can play Lukashev, but the rest is all impacted by Your Honor's decision today.

THE COURT: Okay. You need it before we start tomorrow morning.

MS. BLOODWORTH: We won't play all the dep designations tonight if Your Honor has not ruled yet.

THE COURT: Okay. I do understand why they would want a chance to file a response brief. Just one round makes sense. So if you want to do that and -- if the associate is going to be working -- I'm sorry. I will allow it. Okay? Is that you?

MR. COPLAND: Your Honor, you're correct, the ultimate weight, it could be discarded all at decision time. Couldn't it just be handled in a posttrial briefing. They've objected, the Court defers, and in the posttrial briefing we fully address the issue, both sides, giving all the background necessary for what the federal circuit has been doing, whatever that may be.

THE COURT: Is that your final position on it or --

MR. COPLAND: I threw that out, Your Honor. I apologize. I shouldn't have spoken.

THE COURT: That makes sense. But I feel like since I did look at Biogen's brief, I'm not ordering that you all file something. If you would like to, I'd like to have it as quickly as possible so that I can do that. And yes, it's going to be briefed posttrial if I let it in. I understand that.

MS. BLOODWORTH: Thank you, Your Honor.

THE COURT: All right. Thanks very much.

(Proceedings in chambers conclude at 12:30 p.m.)

(In the courtroom at 1:30 p.m.)

THE COURT: Good afternoon. And, as we get underway, I just want you to understand that I know everybody is set up here. And if you want to stay here tomorrow and as long as we go next week, I'm fine with that. It's up to you where we go. You can direct me at the end of the day if you know. I realize you're all set up and it may be more of a burden to move than to not.

Okay. So we're ready to continue.

Ms. Bloodworth.

MS. BLOODWORTH: Thank you, Your Honor. I'd like to introduce my colleague Ms. Greb, who is going to introduce the first witness.

THE COURT: Good afternoon, Ms. Greb.

MS. GREB: Good afternoon, Your Honor. Mylan would like to call Dr. Matvey Lukashev by video designation. We have prepared some binders as well. We'll pass those out.

THE COURT: Yes. Thank you.

MS. GREB: Your Honor, Dr. Lukashev was a Biogen employee, an inventor, and an inventor named on the original application that issued as the '514 patent. He'll be testifying regarding his work, his relation to Biogen's DMF product, and the discovery research that led to the '514 patent.

For the record, the exhibits that will be referenced during

the testimony are Lukashev Exhibit 1, which is JTX 2195; Lukashev Exhibit 2, which is JTX 2196; Lukashev Exhibit 5, which is DTX 1627; Lukashev Exhibit 6, which is JTX 2000; Lukashev Exhibit 7, which is JTX 2182; Lukashev Exhibit 8, which is DTX 1167; Lukashev Exhibit 9, which is DTX 1016; Lukashev Exhibit 10, which is DTX 1017; Lukashev Exhibit 11, which is JTX 2181; and Lukashev Exhibit 12, which is DTX 1019.

Thank you.

THE COURT: All right. Thank you. 2196, the first one, that's a JTX, right? Just want to make sure.

MS. GREB: Correct, Your Honor.

THE COURT: Okay. Thanks.

(Video played and reported as follows:)

Q. Can you state your name for the record, please.

A. Matvey E. Lukashev.

Q. And what is your home address?

A. It's currently 75 Mechanic Street in Upton, Massachusetts.

Q. I just want to go over a little bit of your background.

Can you tell me what postgraduate degrees you have?

A. It's just one. It's a Ph.D.

Q. What was the topic of your Ph.D. studies?

A. The regulation of endothelial cell morphogenesis. The specialty is essentially molecular and cell biology, if that's what you're interested in.

Q. Then, after your studies at Johns Hopkins, you said you

went to UCSF?
A. Correct. Department of medicine.
Q. The department of medicine?
And what was the subject of your studies at UCSF?
A. Mechanism of function of integrins. They are a family of cell adhesion receptors involved in cell attachment migration and intracellular signaling.
Q. And how long were you there for?
A. I had more than one appointment there. So I left UCSF in the fall of 1998.
Q. And did your research at UCSF focus on the treatment of any particular diseases?
A. Not directly, no.
Q. And where did you go in 1998, when you were done with UCSF?
A. To Biogen.
Q. What was your role when you first started at Biogen in 1998?
A. If by "role" you mean my title, it was scientist II.
Q. And were you hired to do any particular research when you started?
A. Yes.
Q. And what research was that?
A. Initially, it was to help run the angiogenesis program at Biogen and to help, I guess, establish and move forward the functional genomics program.

Q. So after your work on angiogenesis, did you transition to a new project?

A. Yes.

Q. And what project was that?

A. It was focused on informing -- on elucidating the molecular mechanisms of action informing the preclinical development and initiation of the clinical developments of an agonist antibody targeting what's called lymphotoxin beta receptor. LCBR is the standard gene symbol, since you're typing. It's only four letters. And that was intended to be -- that was a molecule pursued as a candidate therapeutic for the treatment of solid tumors.

Q. When was your first project at Biogen that was relevant to the treatment of multiple sclerosis?

A. Directly, it was what at the time had the internal code name BG-12 and eventually became Tecfidera.

Q. And your work on BG-12, when did that start?

A. Again, I cannot give you the exact dates. I believe it was sometime -- I was asked to join the program, I think, sometime around the end of 2005, if I remember it correctly. Could have been early 2006, but I think it was more likely the end of 2005.

Q. What did you understand your role would be on the project when you were asked to join in 2005?

A. Initially, assessments of the information -- of the

mechanism of action information available for the asset we were considering for potential acquisition from Fumapharm. They had a -- they had a data package generated by their collaborators.

Q. So your first involvement with BG-12 was in connection with evaluating the BG-12 asset in connection with the potential acquisition of Fumapharm?

A. It wasn't BG-12 yet because we didn't -- we didn't acquire it at the time yet. So it just -- it was about visiting Fumapharm and reviewing the portion of their data package that related to what they had in the way of mechanism of action. There wasn't much, frankly.

Q. Did you understand that there was an existing license agreement between Biogen and Fumapharm relating to dimethyl fumarate?

A. I wasn't aware of that. And, frankly, it was not my focus. My task was to elucidate the mechanism of action. I represented strictly discovery research in this program.

Q. Were you in any way involved with the clinical trials of BG-12?

A. Indirectly, as a part of the program project team. I was present for some of the discussions, but not -- I was not involved in clinical decision-making. That's not my specialty.

Q. Did you know that Biogen had been conducting a Phase 2 study on BG-12 starting in 2004?

A. Actually, I didn't know -- I did not know that simply

because it was completely outside of what I was working on in 2004. I really became aware of the key happenings within the program after I was asked to join it.

Q. Okay. So I guess your first role on the project was to analyze the mechanism of action of what became BG-12?

A. Correct.

Q. And at that time you were unaware of the clinical application of BG-12?

A. At what time specifically? It's just if it's about the time -- the first time I was asked to join the program, then the answer is I did not. As I said, I was not aware of the ongoing clinical development. But, obviously, I became aware of it as I became a part of the program project team.

Q. What did you understand was the extent of work that Fumapharm had already done on dimethyl fumarate?

A. I, frankly, didn't -- well, again, my focus was on the mechanism of action, and that was superficial. The body of data they had accumulated as mechanism of action data was very thin and superficial at best.

As far as the extents of their -- the work they had done outside of that, I, frankly, wasn't paying much attention. And so -- and it's a little difficult for me to dissociate what I know now from what I knew at the time. I know what I was paying attention to.

Q. So, based on what you know now, what had Fumapharm already

done at the time that you became involved in the project?
A. It's a little difficult for me to answer the question as phrased because, as I said, I cannot remember the exact timing of my becoming aware of various aspects of that. I do know -- what I believe I know is that there was work done in psoriasis and there was a small clinical study, but I can't remember who sponsored it, with DMF in a small cohort of MS patients that unexpectedly produced an interesting clinical signal, which was what prompted our interest in the asset.
Q. So at the time that you were considering the BG-12 asset, there was -- there were clinical studies of dimethyl fumarate in psoriasis and multiple sclerosis that were promising; is that right?
A. As I mentioned to you, I was not focusing on that side of things, and I cannot remember whether -- even to this day, actually, I cannot tell you when the psoriasis work was being done relative to the timing of my involvement with the program. As I said, I became aware of those events as I was spending more time with the program. But my initial focus -- actually, my focus throughout my affiliation with the program was on the mechanism of action.
Q. I'm handing you what's been marked as ML Deposition Exhibit Number 1.
Have you seen this before?
A. This looks like my LinkedIn profile probably.

Q. That's my understanding. I wanted to confirm that. Does this look like your LinkedIn profile?

A. It does.

Q. Does this accurately depict your professional history?

A. I believe it does.

Q. Okay. So, if you could go to -- under your work at Biogen, the senior scientist title.

A. Yes.

Q. And it says Biogen Idec 2003 to 2006 for three years.

Do you see that?

A. Uh-huh.

Q. And then it says BG-12 Tecfidera research lead, since 2005; is that right?

A. Yes, it does.

Q. And that's consistent with your recollection as to when you became involved with BG-12?

A. Yes. Uh-huh, it is.

Q. And did any of your research in 2003 to 2006 time frame involve clinical studies?

A. During this period, I cannot remember. I cannot remember whether -- actually, let me think.

No. We did -- within my group we did not do any work involving clinical samples. That was done by a different function. So -- and during this time I could have been -- could have been, but I don't want to speculate -- involved in

planning discussions with added functions, but no direct work was ever done within my group with clinical samples.

Q. Okay. So, during your whole time at Biogen, you were not involved with the clinical studies?

A. Not directly, no.

I'm sorry. I'm referring -- just to finish the answer, I'm referring to the work done within my laboratory.

Q. Okay. Did you contribute to the clinical development of BG-12 outside of your laboratory?

A. Could you specify "contribute"?

Q. I guess, you know, what is your understanding of your contributions to the clinical development of BG-12?

A. Let me try to answer this. Elucidation of the MOA was molecular -- mechanism of action -- was initiated to provide a section of preclinical pharmacology data that would facilitate a development team's discussions with regulatory agency and so forth because the agency expected to see a certain depth of the understanding of how the drug candidate was working, what was the -- what were the underlying mechanisms of its biological activity. That was the initial main focus.

And, obviously, this type of information needed to be relayed to the rest of the program project team, and the team did involve the clinicians. What use, if any, they made or didn't make of this information, I do not know.

Q. Okay. Did your -- did you have any other contributions to

the clinical development of BG-12 other than providing studies and information on the mechanism of action of it?
A. No, not really.
Q. And you're not a medical doctor; is that correct?
A. No, I'm not.
Q. What is a mechanism of action?
A. It is a mechanism of action. It is really a description, obviously, fact -- scientific fact-based description of the molecular and cellular events affected by the drug -- by the active substance of the drug.
Again, everything we were doing was not really with the drug itself. It was just with the active substance. We did not work with a pill. We did not work with the contents of the pills. We worked with the active ingredient within my group.
Q. Okay. So your work was independent of the actual -- the formulation of the drug and was limited to the active --
A. That is fair to say, yes. It was a separate line of work.
Q. And was your work also independent of the dose of the formulation?
A. Essentially, yes.
Q. Have you determined BG-12's mechanism of action?
A. To an extent, yes.
Q. Can you explain that qualification.
A. In reality, one never knows the entire mechanism of action, the entire scope of molecular and cellular events affected by a

drug once the drug is administered. The system is always too complex for us to know everything we do. That is why clinical development is unavoidable and completely essential part of the development process.

So everything that you call the mechanism of action is always to an extent. There's only a certain depth of the understanding one can achieve. And this is defined by the availability of experimental models. We cannot really truly fully analyze what happens in the human body. So we can attempt to approximate certain events, but it's always work with models. That's why I said "to an extent." It always is to an extent.

Q. So, I guess, to what extent did you understand the mechanism of action of BG-12?

A. We were able to determine that the drug was -- or the active ingredient, rather, was capable of activating the cardinal components of what's called the Phase 2 detox mechanism, that the primary targets of the active ingredient, the one that, again -- actually, I have to say at least one of the primary targets with which the drug interacted directly was the protein called KEAP1. And that interaction led to the activation of a transcription factor called NRF2, which is the master regulator of the mechanism I mentioned earlier as the Phase 2 detox response.

Basically, NRF2 activates -- it's a master regulator of a

whole -- of a fairly large set of genes, all of which serve the purpose of detoxifying electrophilic substances out of the system.

Q. So is it fair to say that you discovered that BG-12 operates through this NRF2 pathway?

A. Not entirely. What we did contribute was the discovery of the fact that the active ingredients of the drug candidate was interacting with this mechanism and activating it. That's really what we contributed.

Q. So you discovered that dimethyl fumarate was interacting with the NRF2 pathway?

A. With its key regulator, called KEAP1, which results in the activation of the NRF2 pathway.

Q. And were you the first to do that?

A. To the best of my knowledge, we were the first group to identify that and eventually publish it as well.

Q. Okay. And if you could go to your LinkedIn profile from that passage we were just looking at, and it says "Developed MOA-based rationale for potential new indications, combination therapy uses, and follow-on compound identification."

Do you see that?

A. Uh-huh, I do.

Q. So now it says "Developed a mechanism-of-action-based rationale for combination therapy uses"?

A. Uh-huh.

Q. Can you explain that to me, please.
A. Again, the part we're talking about is largely hypothetical with very minor amounts of experimental follow-up. Rationale development is really about forming a logical hypothetical motivation for certain types of experimental follow-ups, whether or not you actually conduct the studies.
So, as far as combination therapies are concerned, the literature available at the time was suggestive of a potential utility of combining NRF2 modulators with other types of immunomodulatory agents. And it's fairly easy to construct a case for a number of them, but we didn't do any experimental work. It's just that this was really motivated by the striking phenotype of the NRF2 knockout animals.
Q. Okay.
A. And if you try to -- sorry. If you try to get into the biology of individual immunopathologies, you can construct the case, for instance, for the combinations with T-cell modulators or B-cell modulators, that sort of thing.
Q. You had evidence that dimethyl fumarate was relevant to this NRF2 pathway, correct?
A. Correct, yes.
Q. And these immunomodulatory drugs or other drugs that were used to treat MS and other immune diseases; is that right?
A. I'm afraid that's fair because you -- when I was saying -- when I was commenting on the broad spectrum of immunomodulatory

diseases, that was not specifically MS-related. If you are looking for a specific example of a rationale within an indication, I can describe one as an example, but it will take time because --

Q. Okay. So it was broader than just MS?

A. It was broader than MS. And I can tell you that one possibly logical case for evaluation of MS in an immune-mediated disease, based on our -- the combination of our own data and the literature, could be in the rheumatoid arthritis. And I can explain why, but it will take a long time.

Q. And the thought was that you could combine a drug like dimethyl fumarate that works on the NRF2 pathway with another drug that's known to work on a different pathway for the relevant disease you're looking at?

A. Correct. Yes, by the way of complementary therapies.

Q. Did you do any work to identify a combination of dimethyl fumarate with any other drug that worked with a different mechanism of action?

A. No. As I stated before, our focus throughout my involvement with the program remained solidly on dimethyl fumarates within one indication.

Q. Can you describe the details of the follow-on program for compound identification that you conducted relating to the NRF2 pathway?

A. Yes. The focus of the program was on the identification of small molecules capable of activating NRF2 without being covalently reactive with proteins in general.

You see dimethyl fumarate binds KEAP1 and, in fact, some other proteins as well covalently, and there are potential downsides to this mode of action.

So we, I believe, were the first to attempt the discovery of small molecules that would noncovalently insert themselves into the interface between KEAP1 and NRF2, thereby causing dissociation of the complex and thus allowing the activation of NRF2.

So it's still the same pathway, but you're engaging it in a very different way, and you're not covalently reacting with anything. It's reversible. That was the -- one of the main focus of that effort.

Q. Okay. So based on your work studying the NRF2 pathway mechanism of action, you were looking for other compounds that could work under that pathway; is that correct?

A. It is correct.

Q. And that work was not focused on DMF. It was other compounds, correct?

A. Completely other chemical classes.

Q. Is it fair to kind of refer to this as compound screening?

A. Yes, it is.

Q. Did you screen any compounds other than dimethyl fumarate

for NRF2 activity prior to 2008?
A. No, not -- no, I don't recall anything of the sort, no.
Q. Okay. So this development of a mechanism-based rationale for potential new indications, combination therapy uses, and follow-on compound identification was outside the auspices of the BG-12 program development?
A. Yes, that is correct. As I just said, it was of a more exploratory nature. It's to explore potential for follow-on compound discovery, perhaps movement into other indications or perhaps not previously explored in the clinic in any therapeutic context, combinations of fumarates with other therapeutics.
Q. Did you have any involvement in selecting the dose of BG-12 to be used in clinical trials?
A. Not really.
Q. What do you mean, not really?
A. Define "involved."
Q. Did you provide any input on what dose of BG-12 should be tested clinically?
A. I did not provide any clinical input. That's outside the scope of my expertise and responsibilities at the time.
Q. And, from your work studying the mechanism of action with the active ingredient, is there any way that that can be extrapolated to a clinical dose of dimethyl fumarate?
A. No. Inherently, what one does in research is not designed

or applicable to inform clinical dosing. A good deal of downstream preclinical and clinical pharmacology work needs to be done to arrive at those types of choices, and those are work -- and that is work done by other functions, not by research.

Q. And did you do any studies on the therapeutically effective dose of BG-12 in any disease?

A. Hard for me to say because, you know, we did do experiments with a range of end concentrations of dimethyl and monomethyl fumarate in vitro, but they were really concentrations not meant to precisely represent the clinical exposure levels. There were ranges of concentrations selected, essentially, to examine details of the molecular events that could be, in principle, triggered by the active ingredient in a cell.

Q. So it was never the focus of your work to inform the clinical dosing of dimethyl fumarate?

A. Correct.

Q. Welcome back, Dr. Lukashev.

I'm handing you what's been marked as ML Deposition Exhibit Number 2. This is your copy. Give you time to take a look.

Do you recognize this document?

A. Looks like one of those agenda emails we were receiving as a part of the program team operation.

Q. Is this a copy of BG-12 program team meeting minutes from June 8th, 2006?

A. That's what it says.
Q. And did you receive BG-12 team meeting minutes when you worked at Biogen?
A. I did.
Q. And were these regularly kept at Biogen as part of their business?
A. They were.
Q. Now, I think it says under "PT attendees," I see your name there. Is that right?
A. Where is my name? Yes, it does say my name.
Q. Does that mean that you were present at this meeting on June 8th, 2006?
A. I had to be if I'm on the agenda.
Q. Then under "Agenda" it says "MOA review and discussion of next steps, Matvey." Is that right?
A. It does say that.
Q. Can you explain to me why the mechanism of action of BG-12 was important at this time in June 8th, 2006.
A. I'm not sure how important it was. It was requested by the team.
Q. Is this around the time that the acquisition was completed?
A. To the best of my understanding, yes, somewhere around that time.
Q. And was the pathway unclear at that time?
A. Very little information available to us in the form of an

almost random collection of very small decks. Those studies were conducted by a small network of Fumapharm collaborators without, you know, much coordination. Everyone basically did what was convenient for them to do, and it did not converge into a consistent MOA.

Q. So I'm handing you what's been marked as ML Deposition Exhibit Number 5. And I'll represent to you that this is a document that is part of the litigation here, and it's called our notice of 30(b)(6) topics, which is what we've asked Biogen to give testimony on.

And it's been represented to us that, if you could go to page 5 of this document, that you are here to give testimony for Biogen in relation to Topic Number 11 at page 5.

And so I just wanted to -- you to take a look at Topic 11. It says "Any documents, data, or other information underlying the disclosure, including the examples in the specifications of the patents-in-suit."

Do you see that?

A. I do.

Q. And do you understand that you are here to give testimony on behalf of Biogen on that topic?

A. I believe I do.

Q. Was it discussed that you would give testimony on behalf of Biogen on this topic?

A. That's been my general understanding all the time,

basically, since I was initially contacted.

Q. Okay. So let's take a look at the patent.

I'm handing you what's been marked as ML Deposition Exhibit Number 6. And so is this U.S. patent 8,399,514?

A. That is what it says on the title page, yes.

Q. And is this -- I'll represent to you that this is the patent that's at issue in this litigation.

A. Uh-huh.

Q. And are you listed as an inventor on this patent?

A. I am indeed.

Q. So if you could go to the examples in the patent at -- starting at Column 19.

A. Yes.

Q. And do you see how there are three examples in this patent?

A. Uh-huh. I do.

Q. Did you write these three examples?

A. I had to have provided the drafts, but I cannot tell with certainty whether this is the language of the drafts or it was modified. In all likelihood, it was actually written in its final form by an attorney who was preparing the patent.

Q. But do you believe that you provided the information that the attorney wrote these examples based upon?

A. That would be correct.

Q. And so if you look at Example 1, it relates to an in vitro experiment; is that right?

A. That's correct.
Q. Can you explain what the results of that experiment show.
A. This would require us moving to the Figure 1 mentioned here.
Q. Okay.
A. But over -- I mean, the summary is simple. Example 1 really provides evidence of NRF2 activation by DMF. And what did we have on this figure? We did experiments with both DMF and MMF, but let's see what's on Figure 1.
I'm mumbling because I'm fingering through. I won't repeat myself. I was going to say -- I was saying that we -- yes, we did -- okay. So this did include -- this Example 1 provides evidence of NRF2 activation in a cell-based system by the active ingredient and by its primary metabolite, DMF and MMF respectively.
Q. Okay. So this was an in vitro test in which you found evidence of activation of NRF2 with dimethyl fumarate and monomethyl fumarate?
A. That is correct.
Q. And does that relate to the mechanism of action of dimethyl fumarate and monomethyl fumarate?
A. I believe it does.
Q. And so then is Example 2 another in vitro test?
A. Yes, it is.
Q. And what did the results of Example 2 show?

A. They verify the specificity and the validity of our findings shown in Example 1. This was -- and verification was done by -- with the help of selective elimination using inhibitory RNA constructs, selective elimination of NRF2, or KEAP1 to mimic either simply elimination of NRF2.

So, if you eliminate the biological effects you consider to be evidence of, the pathway activation should disappear, and it does. Conversely, if you eliminate KEAP1, which is a inhibitor of NRF2, you should observe the activation of NRF2 and similar to the activation you observe with the pharmacological activator pathway.

And that is what's shown here as well. And we can go through all the columns if you'd like.

Q. Okay. So this example is another in vitro test demonstrating --

A. Yes.

Q. -- that dimethyl fumarate acts through the NRF2 pathway?

A. Not through, but that it does indeed activate NRF2 and likely through a KEAP1-dependent mechanism, which that latter part was verified later.

Q. Is Example 3 an in vivo test performed in mice?

A. It is.

Q. And that involved administering dimethyl fumarate and monomethyl fumarate to mice?

A. It did.

Q. And what did the results of that Example 3 show?
A. Increased abundance of NRF2 detectable by histological staining in the animals treated with DMF or MMF compared to the control ones.
Q. And did that provide evidence of monomethyl fumarate and dimethyl fumarate activation of NRF2 in vivo?
A. It did.
Q. So is it fair to say that all three of these examples are preclinical experiments directed at the mechanism of action of dimethyl fumarate and monomethyl fumarate?
A. Yes, that's fair to say, with one qualification. In Biogen's organizational structure at the time, "preclinical" was the term referring to specifically a certain function that was downstream of discovery research.

Preclinical, in that context, was about thorough evaluation of this type of discovery data for the purposes of actual preclinical development, really preparing the molecule for the movement into the clinic.

But in the general sense, yes, this was prior to the clinic.
Q. You're just saying that these three examples were part of your research, which was separate from preclinical development component that happens later at Biogen? Is that --
A. That is correct.
Q. So it's fair to say that none of these examples relate to

any clinical application of dimethyl fumarate?
A. Not really. Not directly at all.
Q. And none of the examples involve the clinical treatment of multiple sclerosis?
A. No.
Q. Are you aware of any other data other than Examples 1, 2, and 3 in this patent?
A. No, not in this patent.
Q. And do you believe that the data in Examples 1, 2, and 3 indicate that DMF would be effective in treating multiple sclerosis in humans?
A. The nature of the data is such that it's on a different subject, really. It's nothing to do with the efficacy in clinical disease.
Q. Okay. And do you believe that the data in Examples 1, 2, 3 indicate that dimethyl fumarate would be effective in treating multiple sclerosis in humans at any particular dose?
A. No. This does not in any way follow from the specific set of data.
Q. And do you think this data in any way is helpful in identifying a therapeutically effective amount of dimethyl fumarate?
A. My personal opinion is, no, it doesn't. As a broader comment, this type of data is never directly informing for the purposes of selecting therapeutic dose. Not the right models,

not the right settings, not the right experiments for that purpose.

Q. Okay. And if you could go to Claim 1 of this patent. It's at Column 27.

A. Yes, I'm there.

Q. And do you see how it says "A method of treating a subject in need of treatment for multiple sclerosis comprising orally administering to the subject in need thereof a pharmaceutical composition consisting essentially of a therapeutically effective amount of dimethyl fumarate, monomethyl fumarate, or a combination thereof and one or more pharmaceutically acceptable excipients wherein the therapeutically effective amount of dimethyl fumarate, monomethyl fumarate, or a combination thereof is about 480 milligrams per day."

Do you see that?

A. I do.

Q. What part of this Claim 1 is your invention?

A. Yes. I'm not sure what "invention" means. But, generally speaking, this was a clinical part, and I'm not a clinician.

Q. Claim 1 is directed at a method of treatment, correct?

A. Correct.

Q. And your work was not directed at a method of treatment; is that right?

A. Not explicitly. Not directly. That was the responsibility -- so that was really within the scope of

responsibilities of the clinical department.
Q. Okay. So you weren't involved in the idea of using dimethyl fumarate to treat multiple sclerosis, correct?
A. Yes. What does "involved" mean? I was not the source of the idea. It was not my idea. I wasn't the one who proposed that specifically.
Q. And it wasn't your idea to administer any particular dose of dimethyl fumarate to humans?
A. No. And it could not have been because this is outside the realm of my expertise or responsibilities -- job responsibilities at the time.
Q. Before 480 milligrams ended up working -- before you got the results or heard the results of that, did you have any expectation as to whether that dose would work or not?
A. No. That could only have been determined in the course of clinical developments.
Q. Which you were not involved in; is that right?
A. No. That was the job of the clinical members of the program team.
Q. I'm handing you what's been marked as MK Deposition Exhibit Number 7.
A. ML? You wanted to say ML, right?
Q. You're right. ML Deposition Exhibit Number 7. And it is a document that is Bates numbered DEF-DMF 0011425 through 11472.
A. Uh-huh. Yes.

Q. And so -- and, if you look at the second page of this document, and this is -- this is what the patent office puts on certified copies of documents. And it says "Application Number 60/888,921, filing date February 8th, 2007."

About halfway down.

Do you see that?

A. The second page is the one with the picture on it?

Q. Yeah.

A. Page number --

Q. So it says "This is to certify that the annexed hereto is a true copy from the records of the United States Patent and Trademark Office of those papers of the below-identified patent application that met the requirements to be granted a filing date." And then it refers to an application filing date.

I just want you to confirm that this is the provisional application referred to in your patent.

A. I do see what's on this page, yes.

Q. Okay. And were you involved in preparing this application prior to its filing on February 8th, 2007?

A. I was to the extent to which I provided the original data and initial discussions with the attorney preparing this application.

Q. And who was the attorney that was preparing this application?

A. Konstantin Linnik, double N. It's L-I-N-N-I-K, Konstantin,

which is the Russian spelling of it. It's K-O-N-S-T-A-N-T-I-N.
Q. Are you aware of any involvement that -- first of all, do you know Gilmore O'Neill?
A. Yes, I do.
Q. Are you aware of any involvement that he had in this patent application?
A. I know he is one of the inventors listed here. And so his involvement in the generation of the patent itself is -- the extent or forms of it are unknown to me.
Q. Do you know why he's listed as an inventor?
A. I don't.
Q. Was he involved in any of the work that you did that you provided for the examples?
A. No.
Q. So your thought was that you could use the knowledge of dimethyl fumarate's mechanism of action to screen for other compounds that acted under that mechanism; is that right?
A. That is fair to say.
Q. And so the title on page 1, "NRF2 Screening Assays and Related Methods and Compositions," do you see that?
A. Yes, I do see it.
Q. And is that referring to NRF2 screening assays that could be used to identify compounds beyond dimethyl fumarate?
A. That was the intent here.
Q. And at paragraph 30, it says "Due to the involvement of

NRF2 in the regulation of cellular response to metabolic stress, survival, and inflammation, DMF, MMF, and other NRF2 activators may be useful for therapeutic management of a variety of inflammatory, ischemic, and neurodegenerative processes."

Do you see that?

A. Yes, I do.

Q. And, again, is this explaining that the -- that the function of DMF and MMF in this NRF2 pathway provided an indication that other NRF2 activators may be useful?

A. I mean, that is essentially what we were thinking at the time.

Q. Did you believe that you provided a rationale for the use of dimethyl fumarate in combination therapy?

A. At the level of discovery research, yes.

Q. Did you believe that you provided a rationale for a means of identifying compounds that worked in the NRF2 pathway?

A. Yes, for discovery research purposes.

Q. And what do you mean by "discovery research purposes"?

A. When we -- to me, when we start talking about compounds for treatments, it implies the availability of a certain body of data and that illustrates utility for actual treatment, and that requires clinical data.

So none of which -- and the clinical part of or the formerly preclinical were not provided by me in any shape or

form. So this is strictly for discovery. This is really a rationale for a method of discovering them, like, at the early stage.

Q. So your ideas were to use this as a discovery tool?

A. Correct.

Q. And it could be used as a discovery tool in a variety of ways to identify new compounds; is that right?

A. New chemical entities, yes.

Q. And new combination therapies with NRF2 drugs; is that right?

A. I'm reluctant to cross the bridge between candidates and actual therapies. Therapy needs to be evaluated in the clinic; candidates can exist in the research domain.

Q. And, as a method for identifying applications in other indications?

A. More as a method of -- in that context perhaps as a method that could -- no, actually, in this patent, what you just said did not follow directly from the data. But the type of -- this type of data could be used to generate preliminary suggestions of potential applications but not to sufficiently inform the application per se.

Q. If you could go to paragraph 73. It's on page 16.

A. Yes.

Q. And it says "In some embodiments of Methods 1 through 5, the compounds that are being screened, identified, evaluated,

or used for treating a neurological disorder are mild alkylating agents and, more specifically, Michael addition acceptors or compounds that are/is metabolized to Michael addition acceptors."

Do you see that?

A. Yes.

Q. How did you conceptually identify this class of compounds of interest?

A. That was motivated by the data we generated using dimethyl and monomethyl fumarates, because they are both minimal Michael acceptors.

Q. Okay. So you thought other Michael acceptors might have the same properties?

A. Correct.

Q. And so this was about identifying compounds other than the dimethyl fumarate and monomethyl fumarate for activity in NRF2?

A. Yes. That was for identification of novel compounds.

Q. And I think from paragraph 74 through 84 goes through a recitation of potential compounds. Is that right?

A. Correct.

Q. And do you know how many compounds that encompasses?

A. I do not.

Q. Is it fair to say that's a vast number of compounds?

A. I think it's not a knowable a priori number of compounds.

Q. And the purpose of this disclosure is to provide a chemical

space of compounds to conduct the screening to identify novel compounds, correct?
A. That is correct.
Q. And in screening for these novel compounds, other than dimethyl fumarate and monomethyl fumarate, the thinking was that those could potentially be useful for a number of different diseases?
A. That is correct.
Q. And if you could go to 11 -- sorry. It's page 28, the heading "Neurological Diseases."
A. Yes, I'm there.
Q. And so I guess, starting at paragraph 104, it says "A neurological disease in Methods 1 through 5 above can be neurodegenerative disease such as, for example, ALS, Parkinson's disease, Alzheimer's disease, and Huntington's disease. The neurological disease can also be multiple sclerosis or other demyelinating diseases of the central or peripheral nervous system."
Do you see that?
A. I do.
Q. And are these the potential diseases that the screened compounds could be found to treat?
A. These are diseases in which NRF2 was implicated as a potential pathogenically relevant mechanism.
Q. And so you weren't saying that any of these particular

compounds would actually be useful in treating any of these diseases, correct?
A. I was not asserting that.
Q. These were the diseases that you knew that NRF2 was potentially relevant to?
A. As I stated, that's where NRF2 was implicated as potentially relevant to. "Knowing," to me, means a different burden of proof.
Q. And your patent application didn't provide any additional clinical evidence relating to multiple sclerosis, correct?
A. Correct.
Q. Do you know what patent claims are?
A. In general. I've seen them.
Q. Okay.
A. I'm not sure -- what "do I know" means.
Q. Are you aware that they're used to define the invention?
A. I'm not a legal professional. You see, my familiarity with this is fairly superficial.
Q. Okay. That's fair.
Is it your understanding that these claims were written to cover the NRF2 screening assays that you had thought about?
A. Yes. Again, I cannot evaluate the full extent and implications of the claims. I can -- as I stated before, I know what the scope of the data that started this application was. I know we provided it. But the legal expansion of that

was outside of my scope of knowledge or responsibility.
Q. And if you could go to page 31 under the heading "Dosages and Formulations."
A. Yes. I see that.
Q. Did you provide any of the information about dosages and formulations that are in this patent application?
A. I did not.
Q. Do you know where it came from?
A. Not really.
Q. What do you mean? Are you unsure or --
A. I'm not willing to speculate who the sources were. This mentions the types of data that I could not have generated -- monkey, dog, humans. Monkeys and dogs are in the preclinical domain, humans in the clinical.
Q. So --
A. I'm talking about Table 2.
Q. You're referring to Table 2.
A. Yes.
Q. And Table 2 "For equivalent surface area dosage factors." Do you see that?
A. Yes, that is the one.
Q. Were you aware that this was in your patent application?
A. I eventually became aware of it.
Q. Have you ever done any sort of converting doses between animals and humans?

A. No. I'm not trained to do that sort of analysis. It requires professional expertise of a pharmacologist.
Q. What is your understanding as to why this section on dosages and formulations was included?
A. I do not know what to say.
Q. You don't have any understanding as to why this was included?
A. I have no knowledge of why. And, again, without the benefit of having read this -- having studied the application recently, I cannot, on the fly, understand why and how this belongs here.
Q. Do you believe that the data obtained in the NRF2 mechanism of action assays can be used to formulate a range of dosages for use in humans for the compounds disclosed in this patent application?
A. The data incorporated into this application cannot be used to define clinical dosing.
Q. Are there any therapeutically effective doses indicated in the examples?
A. You mean the 1 and 2? No.
Q. Are you aware of anywhere in this patent application that identifies specific therapeutically effective dosages?
A. Specific therapeutically effective dosages. Yes, it is a bit vague. As of 15 seconds ago, I am simply because I just glanced at 116 and it does mention 480 or 720 milligrams per

day. So that's what -- so I am now.
Q. So you're referring to paragraph 116 on the next page?
A. Yes. This is where it mentions a range of doses, including 720 milligrams per day and 480 to about 720.
Q. But, again, that's a range of dosages between 480 and 720, correct?
A. It is, but including.
Q. And there's only one specific dosage that's mentioned there, 720 milligrams per day, correct?
A. I would not interpret it this way because, when the range delimited by two specifically mentioned numbers is defined, those numbers are mentioned, correct?
Q. And from this disclosure are you able to determine that any particular dose of dimethyl fumarate or monomethyl fumarate is therapeutically effective?
A. I cannot make that determination in principle. I'm not a clinician, and I cannot derive it from the language of this disclosure.
Q. And then in the last sentence -- or the second-to-last sentence, that describes a range -- an effective dose of DMF or MMR -- I think that's a typo -- MMF to be administered to a subject orally can be from about .1 milligram to 1 milligram per day, I think.
Do you see that?
A. I do.

Q. And, again, that discloses a range of amounts of these drugs that could be administered per day, correct?
A. This is what it appears to be saying. But, again --
Q. And do you believe that .1 milligrams -- or .1 -- is that 100 milligrams? Do you have any understanding as to whether 100 milligrams of dimethyl fumarate is therapeutically effective and --
A. I don't know.
Q. Is there anything in this paragraph that identifies a preferred dosage for dimethyl fumarate or monomethyl fumarate, from your perspective?
A. Preferred by whom?
Q. By you, the inventor.
A. I did not invent the clinical dosing.
Q. Handing you what's been marked as ML Deposition Exhibit Number 8. And do you see how, in the upper left-hand corner of this document, Item 21, it says "International Application Number PCT/US2008/001602"?
A. I do see that.
Q. And then it has an international filing date of February 7th, 2008, directly under that?
A. I do see that as well.
Q. And then it has -- Item 30 says "Priority data, 60/888,921," and that's reference to the provisional patent application that we had just looked through.

A. This one?
Q. Is that right?
A. That's what it says here.
Q. And it says "Filed by applicant Biogen," and then it lists as an inventor "Lukashev, Matvey." Is that right?
A. Correct.
Q. Handing you what's been marked as ML Deposition Exhibit Number 10, and I'll represent to you it's Bates number DEF-MMF 0010986 through 10987. And I'll represent to you it's another document that we obtained from the patent office.
And do you see how it says "Combined Declaration and Power of Attorney" at the top?
A. It does.
Q. And is this document signed by you?
A. This does look like my signature.
Q. And is that dated December 6th, 2010?
A. That's what the -- that's what is written on the page.
Q. Did you review this declaration and power of attorney?
A. Yes, of course.
Q. And so the third paragraph down, it says "I believe I am the original, first, and sole inventor of the subject matter which is claimed and for which a patent is sought on the invention entitled 'NRF2 Screening Assays and Related Methods and Compositions.'"
Do you see that?

A. Yes, I see that.
Q. And then it refers to the application that was filed on August 7th, 2009, as Serial Number 12/526,296 that we just referred to, Deposition Exhibit 9, right?
A. The one marked with a cross here?
Q. Yeah.
A. Yes, I see that.
Q. And did you believe that you were the first and sole inventor of the subject matter in that patent application?
A. I do not know the full extent of what it means. To the best of my understanding, I was relevant to this.
Q. At the time were you aware of any other potential inventors that should be listed on your patent application?
A. No.
Q. At the time did you know of anyone else who contributed to the invention disclosed in that application?
A. As I mentioned earlier, the technicians who generated the data were naturally known to me as sources of the data incorporated into this. Other contributions into the language or clinical and -- legal or clinical language, I do not know exactly who contributed those.
Q. And did you believe that, at the time, that Gilmore O'Neill contributed to the invention disclosed in your patent application?
A. As I just stated, I did not know whether Gilmore

contributed to the language or to the clinical. I simply do not know.

Q. When you executed this document in 2010, what did you understand your invention to be?

A. It's -- again, in legal terms, I cannot answer the question. My nonprofessional in a legal sense understanding was that it was what it says, the method of screening, basically, a method of discovery for identification of NRF2-activating compounds, small molecules.

Q. And that invention didn't have anything to do with the clinical dosing of dimethyl fumarate, correct?

A. As the source of the data included in this application, the data did not directly and immediately lead to the selection of clinical -- the data did not immediately lead to and could not directly and immediately lead to the selection of clinical doses.

Q. I'm handing you what's been marked as ML Deposition Exhibit Number 11. And this is a document that's Bates-numbered DEF-DMF 0010947 through 10957.

Do you see that?

A. I do.

Q. And, again, I'll represent that this is another document that we retrieved from the patent office. And do you see how it's in regards to your patent application 12/526,296, the top left?

A. Yes. That's what it says here.
Q. And do you see -- if you go to DEF-DMF 0010953, do you see that it was submitted on June 20th, 2011?
A. That is what it says here.
Q. By an attorney named Marsha Rose from Sterne, Kessler, Goldstein & Fox.
Do you see that?
A. Yes, I do.
Q. If you go back to the first page, it says "In advance of prosecution, applicants submit the following amendments and remarks."
A. Yes, it does say that.
Q. And I think you have to go to the very last page because it was out of order, but I think that that is page 2. It says page 2 at the top.
Do you see that?
A. Yes, it does say page 2, but it's the last page.
Q. And then it says "Amendments to the Title." It says "Please amend the title as follows."
A. Uh-huh. I see that.
Q. And it strikes out "NRF1 Screening Assays and Related Methods and Compositions" and replaces it with "Treatment for Multiple Sclerosis." Do you see that?
A. I do.
Q. And then if you go back to the first page, it says

"Amendments to the claims are reflected in the listing of claims which begins on page 3 of this paper," and page 3 is the next page, DEF-DMF 0010948.

Do you see that?

A. I see that.

Q. And do you see how it canceled all of the existing claims, 1 through 17?

A. That is what it says.

Q. And it put in new claims, 18 through 33?

A. Yes, I do see them. New claims, uh-huh.

Q. And this is at DEF-DMF 001309. Do you see that?

A. Yes.

Q. And then there's 17 claims there. Do you see that?

A. Yes, I do.

Q. And do those relate to the NRF2 screening assay?

A. They do.

Q. And so the claims that are directed to the NRF2 screening assay were canceled, and then new claims that are directed at "a method of treating a subject in need of treatment for multiple sclerosis" were added; is that right?

A. That is what appears to have happened, based on this document.

Q. Do you think you invented anything in these Claims 18, 28, and 32?

A. To the best of my understanding, I don't believe I did, but

to the best of my understanding, simply because these are clinical claims and I am not a clinician.

Q. They don't relate to the work that you were doing on NRF2 screening assays?

A. Not directly and immediately in the technical sense.

Q. And from the work that you were doing on NRF2 screening assays, you couldn't extrapolate a particular dose of 480 milligrams per day, correct?

A. From -- that was impossible to extrapolate directly and immediately from the in vitro data we generated.

Q. I'm handing you what's been marked as ML Deposition Exhibit Number 12, and this is a document that's Bates-labeled DEF-DMF 0007801 through 7826. And I'll represent to you that this is another filing that we retrieved from the patent office that we can walk through.

So do you see how this is in regards to your application, the 12/526,296?

A. That is the application number, the third line on the left? Or, technically, line on the left?

Q. Yes.

A. I see that.

Q. Do you see how this is titled "Supplemental Amendment and Replay under 37 CFR Section 1.111"?

A. I do see that.

Q. And if you go to the Bates label 7808 at the bottom right,

do you see how this was submitted on October 28th of 2011?
A. Yes, that's what it says here.
Q. And if you could go to DEF-DMF 7807, which is the page before.
A. Uh-huh. Yes.
Q. The second-to-last paragraph says "Additionally, applicants submit herewith a request to add an inventor in a nonprovisional patent application under 37 CFR Section 1.48(c), seeking to change the inventive entity from Matvey E. Lukashev to Matvey E. Lukashev and Gilmore O'Neill."
Do you see that?
A. I do see that.
Q. At this point in 2011 were you aware that Gilmore O'Neill was going to be added as an inventor on your patent?
A. I simply don't remember.
Q. Did you ever come to any understanding as to why Gilmore O'Neill was added as an inventor on your patent application?
A. It looks natural to me because, you know, probably because the clinical claims were incorporated.
Q. Okay. So your understanding was that, since the claims were changed to be clinical, that that's why Gilmore O'Neill was added as an inventor?
A. That is my current understanding.
Q. And that's because he's the clinician that worked on dimethyl fumarate; is that right?

A. That is correct.
Q. There's three new -- looks like three new claims, 34 through 36.
A. That does look to be true, yes. Uh-huh.
Q. So the ones that were previously presented that we looked at relating to the 480-milligram dose, you said that, you know, you were not involved in those clinical claims.
Were you involved in these newly added claims?
A. Yes, to the extent to which NQO1 was identified and validated as an end point of NRF2 activation in the work done in my group and in the work we did in collaboration with the preclinical departments.
Q. Do you know whether, clinically, the expression level of NQO1 in a subject is elevated?
A. That was demonstrated by -- so the data was generated, I believe, by our preclinical people simply because it had to be combined and so forth.
And, if I remember correctly, the actual clinical samples used for that purpose -- but I'm not prepared to swear that I do remember precisely. I think those samples could have come from an RA trial. Basically, I did not -- there was clinical development of -- the mainstream program was clinical development of BG-12 in multiple sclerosis. And there was a Phase 2 run in rheumatoid arthritis. We did that as well.
And, somehow, I'm tempted to say that -- but that needs to

be verified. So the clinical samples from which the data was generated showing that NQO1 does move in response to BG-12 exposure, they could have -- those samples could have come from the RA trial. But, again, that's to the best of my recollection. It's easy to find out.

Q. If you could turn back to Deposition Exhibit Number 12, the most recent one. Okay. So in that exhibit, can we go to page 7817.

A. Yes.

Q. So at this point you were signing a declaration that you're a joint inventor.

Did you have an understanding as to why you were now a joint inventor?

A. I believe I did, because of the -- it had to do with the evolution of the document. So it now incorporated the clinical details, which was the dosing, and that certainly required an input from the clinician.

Q. It had to do with the newly added claims?

A. That was my understanding.

Q. So I'm at 7819.

A. Yes.

Q. And it is the second paragraph, the first sentence there.

A. Yes.

Q. You see that first sentence?

A. "Applications bring to the examiner's attention"?

Q. Yeah.
A. Yes, I do.
Q. It mentions a meeting with the FDA on August 30, 2006?
A. It does.
Q. What do you know about that meeting?
A. I mean, according to this, it took place.
Q. Were you present?
A. No. At least not to the best of my recollection.
Q. And do you see on the second sentence, it contains a reference to BG-12 dimethyl fumarate dose of 240 milligrams BID, 240-milligram twice daily, corresponding to a 480-milligram-per-day dose?
A. Yes, I see that written here.
Q. Do you know whether, at the time of the meeting, Biogen was planning to pursue a 480-milligram-per-day dose in clinical trials?
A. I do not. That was outside of my realm of responsibilities.
Q. So, I guess, I think that the three claims that you said you were involved with were the expression of NQO1; is that right?
A. Correct.
Q. Did you perform any experimentation to show that the expression level of NQO1 in a subject is elevated after administering to the subject a therapeutically effective amount

of dimethyl fumarate, prior to August 30th, 2006?
A. My contribution was a bit different from what you just stated. So, technically, the answer to your question is no, but I did contribute in a different way.
Q. And how did you contribute in a different way?
A. My group identified NQO1 as a molecular end point of NRF2 activation. The data was used to inform the experiments conducted in the compliance setting within the clinical department using clinical samples.
And I was involved in, A, the transfer of the candidate biomarkers. That's what NQO1 was for those purposes. To the preclinical and into the design analysis of the data and the experimental design of what was being done to the clinical samples. But the actual physical wet work was performed in the preclinical department.
Q. And if you could turn back to the '514 patent. I think it is --
A. I don't happen to remember the sticker number, exhibit number.
Q. I should keep better track of this.
A. I think I found it. Number 6, right? This?
Q. Yes. So at Column 2, and line 58, are you there? It says "provided."
A. "Provided are methods that comprise"?
Q. "At least one of the following methods"?

A. Yes, I'm there.
Q. So Method 1 is methods of screening at least one new candidate compound for treating a neurological disease; is that right?
A. That's what it says.
Q. And is that referring to your thought of using the NRF2 screening assay to identify new compounds other than DMF and MMF?
A. Correct.
Q. And then Number 2, "Methods of evaluating neuroprotective properties of at least one drug candidate for treating a neurological disease."
Do you see that?
A. I do.
Q. And is that referring to evaluating the neuroprotective properties of those drug candidates?
A. Yes.
Q. And then Method 3 says "Methods of comparing, e.g., for bioequivalence, at least two pharmaceutical compositions which comprise fumaric acid derivatives."
Do you see that?
A. I do.
Q. What are those methods?
A. It is my understanding that Number 3 actually relates to the use of the biomarkers.

Q. Okay.
A. Because you can use them as the end points by the movement of which you can determine the relative activities of different -- of two targeting compounds.
Q. And is that used in screening new compounds?
A. It can be.
Q. And what -- and is the idea to compare new compounds to known compounds like dimethyl fumarate and monomethyl fumarate?
A. Not necessarily. But that is one of the things people often do when they look to improve upon the existing molecules.
Q. But in this context were you referring to using this to screen for new compounds?
A. On both, really, because the same scope of methods is applicable to the bioequivalent studies and to the discovery of new compounds.
Q. Okay. And then Number 4 is "Methods of treating a neurological disease by administering to the subject in need thereof at least one compound that is partially structurally similar to DMF or MMF."
Do you see that?
A. Yes, I do.
Q. So that's referring to other compounds than DMF or MMF for treating neurological disease?
A. I mean, I will say, because I think -- I believe this was related to a part of nascent at the time, really, mostly just

conceived components of the novel compound discovery efforts. So we had actually more than one.

So the more complicated and more, at least initially, labor-intensive one was the discovery of molecules that would target the NRF2 pathway in ways different from the ways in which the fumarates target that.

And the second component was really about the discovery of novel fumarate derivatives. It's really one effort using the same methods, just different chemical classes.

Q. Okay. So this is referring to identifying different compounds that are similar to DMF and MMF in some way?

A. Some of them would be structurally similar; some explicitly not. So --

Q. Okay. So then Number Five is "Methods of treating neurological disease by combination therapy that comprises administration of one first compound that upregulates the NRF2 pathway and at least one second compound that does not upregulate the NRF2 pathway."

Do you see that?

A. Yes.

Q. And so that's directed at combination therapies with a compound that has NRF2 activity and a compound that doesn't, correct?

A. Yes, the search for potential complementary therapeutic applications.

Q. Okay. And so do any of the methods that are described in the claims of this patent at the end, Claims 1 through 20, fall within the categories of the methods that you provide at Column 2?
A. 1 through 12, you said?
Q. 1 through 20.
A. 1 through 20. Yes, as far as 17 and 18 and 19 are concerned. And the reason why is that these methods naturally lead -- they can be used for the discovery, and that was actually illustrated in the original filing. The same methods can be used for the identification of candidate biomarkers, and the NQO1 ended up actually being identified using the same methods.

So your starting point is the same. It's just that you either come in with a known active ingredient or with novel molecules, and you either follow one distinct molecule end point or you engage in the discovery of many.

Q. All of Claims 1 through 20 are for methods of treating multiple sclerosis, correct?
A. I just specifically said that those methods are relevant for the purposes -- can be -- or can be relevant for the purposes of what's mentioned in 17, 18, and 19 specifically.
Q. And so the NQO1 is what you're referring to as being related to the methods disclosed at Column 2, line 58?
A. That is an example of, yes, an end point related to those

methods. And the abundance of NRF2 is another example related to the same.

MS. BLOODWORTH: Thank you, Your Honor. I believe we are finished with Dr. Lukashev's dep testimony.

THE COURT: Okay. This would probably be a good opportunity to take a midafternoon recess for you all, and then we'll come back with what's next? Or is that it today?

MS. BLOODWORTH: Well, Your Honor, the next two would depend upon the Court's ruling from this morning.

THE COURT: Okay. I'm prepared to give you that. Why don't you all take the recess -- well, no. I'll give it to you right now.

I've been -- I have read over the -- I think the two cases on which Mylan is mainly relying, and that would be the Nuvo v. Dr. Reddy's Lab and the Synthes USA v. Spinal Kinetics. And in determining this, as I said earlier, my inclination is to let this evidence in, and then I can always rule it out if, upon my review of all the evidence in the case, I determine that its admission and my reliance thereon would be prejudicial and in violation of the rules of evidence and the rules established for the prosecution of this case.

But it does appear -- and we tried to search out cases relying on Nuvo. None of them relate to the issue before me today. But it does appear, from what the court said in Nuvo, that this evidence should come in and -- because, as Nuvo says,

it, quote, eliminates the absence of critical description in this case.

In determining whether Biogen would be prejudiced here -- and what we're talking about is the admission of the evidence of the discussions within Biogen and the discussions at the FDA, it basically goes to the question of whether the finder of fact may determine that the '514 patent is invalid under paragraph 112 because there is substantial evidence that would support Mylan's argument that the claimed method is not supported by the evidence and whether the sufficiency would be -- if the evidence would warrant a skilled -- a person skilled in the art knowing that the inventor had possession of the claimed subject matter as of the filing date.

What I understand to date is that we're looking specifically at whether the 480 dosing, as disclosed in the patent, is supported by a sufficient written description that would allow that POSA to recognize that the patentee had, at the time of the patent's filing, invented that dosage and had used it such to understand that it had therapeutic efficacy in the treatment of RRMS.

So, if my understanding of the question is that, then I'm going to allow the evidence. And to the extent that what I actually hear persuades me that this is not 404(b) and it doesn't go to motivation or some other admissible issue, then I'll -- I won't rely on it. But I am going to let it come in.

All right? So that's my ruling.

So let's take a 15-minute recess. It's 10 after. Please be back, prepared to resume, at 3:25. Thank you.

(Recess taken, 3:10 to 3:25.)

THE COURT: Debbie thought that perhaps I should clarify for you all. I'm agnostic as whether we go or stay tomorrow, next week, at all. You've got all this technology set up. The temperature is working. I'm fine. I don't have any problem at all, and I hate to see you all go to the extent of having to replicate the technology just to get into a larger courtroom. But, again, the choice is yours. But if I hadn't been clear about that, please understand.

MR. MONROE: With your indulgence, Your Honor, we did talk during the break and I believe came to a conclusion that we would prefer to stay, if that's okay with Your Honor.

THE COURT: That's fine.

MR. MONROE: Have the technology set up. No glitches now. Everything is working well.

MS. BLOODWORTH: It's nice and cool.

THE COURT: Very well.

Then, based on the rulings, are you ready to proceed?

MS. BLOODWORTH: Yes, Your Honor. And, again, Ms. Greb will be introducing the next witness.

THE COURT: Thank you.

MS. GREB: Your Honor, the next witness Mylan will call is

Mr. William Sibold, also by video designation. So we've also prepared some binders. If we could pass those out, please.

Your Honor, Mr. Sibold was the director of new products commercialization, and he will be testifying regarding the commercial group involvement with the dose selection of the Phase 2 studies.

For the record, the exhibits that will be referenced during the testimony are Sibold Exhibit 4, which is DTX 1397; Bozic Exhibit 2, which is JTX 2039; Sibold Exhibit 5, which is DTX 1417; Sibold Exhibit 10, which is DTX 1423; Bozic Exhibit 10, which is DTX 1426; and Sibold Exhibit 11, which is DTX 1439.

THE COURT: All right. Thank you.

MS. MASUROVSKY: Laura Masurovsky on behalf of Biogen.

THE COURT: Good afternoon.

MS. MASUROVSKY: Good afternoon, Your Honor. We have the Court's ruling on the motion.

THE COURT: Of course you object, and your objection is preserved.

MS. MASUROVSKY: Thank you, Your Honor.

May I ask the Court, we would like to maintain our objection to each of the following --

THE COURT: Yes. Continuing objection does not have to be spread on the record. The Court assumes that you are objecting to any testimony related to the basis for the motion in limine.

MS. MASUROVSKY: Thank you, Your Honor.

THE COURT: You're welcome.

(Video played and recorded as follows:)

Q. Good morning, Mr. Sibold.

Where did you go after Clinical Studies, Limited?

A. I went to Biogen in September of 2001.

Q. And how long were you there for? Or when did you leave?

A. I left in around August of 2009. I could be a month off.

Q. What positions did you hold at Biogen? If you could walk through them, we can start with the first one.

A. Sure. And I may have the titles a little off. I'm just trying to remember the titles. But started out as, I believe it was, director of new products commercialization and was there from -- in that role from September 2000 -- pardon me -- yeah, September, yeah, 2001, until August 2004.

And then in August 2004 I moved to Sydney, Australia, to be the head of Australia, New Zealand, and Asia Pacific. Was there until June of 2006 and returned to the role of U.S. head -- vice president, head of U.S. neurology.

And then, subsequent to that, added the title of U.S.A. V.P. of oncology, immunology, and neurology. And that's the title which I left Biogen with in 2009.

Q. Were there any particular therapeutic areas you focused on while you were in Sydney, or were you for all the products that were marketed by Biogen in that region?

A. Yeah. So in Sydney the in-line marketed product, we had one, Avonex, for multiple sclerosis, and we were attempting to get a product for psoriasis reimbursed, by the name of Amevive.

Q. Did you have any involvement with any -- with BG-12 or dimethyl fumarate while you were in Sydney?

A. No.

Q. How about during your time from 2006 to 2009, when you had a couple different positions? Were you involved with BG-12 or dimethyl fumarate during that time?

A. Not directly. It wasn't under my responsibilities. My responsibilities were very focused on approved products. And at the time that was Avonex; Tysabri, which was my mandate coming back from Australia; and Rituxan, through our agreement with Genentech at the time for rheumatoid arthritis and for an oncology indication.

Q. Did you have any indirect involvement with BG-12 or dimethyl fumarate during that time that you recall?

A. I can't recall.

Q. Were you involved in the launch discussions at all? I don't remember when it was actually launched, frankly.

A. No. No, I wasn't.

Q. Outside of your time at Biogen, were you involved with the design of any clinical trials? I'm not suggesting anything about your time at Biogen. I'm just asking about your time outside of Biogen.

A. Not directly, no.
Q. Have you had any particular training in pharmacology or medicine?
A. No. Well, let me say on pharmacology, at Yale I took a single pharmacology class as part of my undergraduate degree.
Q. Anything beyond that?
A. No.
Q. Have you had any training with respect to the science behind the selection of doses for pharmaceutical products?
A. No.
Q. Like to now turn to the BG-12 project.
Are you familiar with that term, BG-12?
A. Yes, I am.
Q. When did you first become involved with BG-12?
A. I just can't recall.
Q. Were you involved in any discussions related to the cooperation with Fumapharm on that project?
A. I had some involvement, yes.
Q. Was it in-licensed at first?
A. I can't recall.
Q. What was your -- during that time frame, where the companies were first discussing cooperating with respect to dimethyl fumarate, what was your role or involvement?
A. In my role as the head of new products commercialization group, it would be looking at an assessment of what -- there

was the market potential and various indications that a product could potentially be approved in. That would be -- that would be the extent of it, as we did with any of the business development opportunities or products within the pipeline at the time.

Q. At that time frame did Biogen have any products that were used or indicated to treat psoriasis?

A. Uncertain of the timing. Amevive had been approved for psoriasis. Can't recall the year; so I'm not sure of the overlap.

Q. And was that product developed by Biogen?

A. I can't recall.

Q. Do you recall if Biogen was initially interested in psoriasis and multiple sclerosis with respect to dimethyl fumarate?

A. Can't recall.

Q. What was your first recollection of your involvement with dimethyl fumarate?

A. I remember a meeting in Switzerland with some members of the management team.

Q. Do you recall what was discussed at that meeting?

A. I don't.

Q. Do you recall if it was before or after any agreements had been reached?

A. I don't.

Q. Do you recall anyone else, off the top of your head, that was on the clinical team for BG-12 MS?
A. The team was led by Al Sandrock, and I believe Mike Panzara was on that team, but I can't recall the details of who the official team was.
Q. Do you know what the role of the clinical group was in the design of the BG-12 Phase 2 study?
A. To design the trial. I mean, look, the clinical team is responsible for the clinical development programs of any of the assets, and they are the ultimate owner of and, really, the decision maker for any clinical development program at the time at Biogen, as I recall.
Q. I've just handed you Sibold Exhibit 4, bearing Bates labels BiogenM10153175. And then there's an attachment. And I'll just note for the record that this is out of Bates label order because we separately received production of the native yesterday. And that attachment is BiogenM101725161.
Is this an email that you sent on February 18, 2004, to your colleagues?
A. Yes, it appears to be.
Q. And the subject is "BG-12 CTRB prep doc."
Is that correct?
A. Correct.
Q. At the beginning of your email you indicate that you have attached a summary of the options being considered for the

Phase 2 MS study and the rationale behind commercial's position; is that correct?

A. Correct.

Q. And you go on to indicate that "Clinical is still pushing for Option 1, which includes 240 milligrams, because it's 'good science.'"

Is that correct?

A. Yes, that's what I've written. Yep.

Q. And if we could turn to the attachment.

Does this identify four different dosing options that were being considered for the Phase 2 MS study?

A. It appears to be identifying options, correct.

Q. And you indicate that clinical preferred Option 1 and commercial preferred Option 2?

A. Yes, from the email, that's correct.

Q. There's a heading lower down on the page, "Commercial rationale for Option 2."

Do you see that?

A. Pardon me. Are we on the attachment?

Q. Correct.

A. "Commercial rationale" -- yes, I see that.

Q. Heading Number 2 states "Would like the MS dose to be comparable to the psoriasis dose, 720 milligrams."

A. Okay.

Q. Is that correct?

A. The sentence is correct. The content of the sentence. So I don't have an opinion on -- can't recall the reason as to why that statement was made.
Q. You go on to indicate that "Testing higher in the range, 360 to 720, is therefore better."
A. Yes, I see that.
Q. You don't have any recollection of why commercial preferred to have a higher dose as opposed to a lower dose for MS?
A. No, other than going back to the first sentence which says they would like the MS dose to be comparable to the psoriasis dose of 720. So I'm assuming that's what the opinion was at the time.
Q. And in Point 3 under that heading you state "This is about risk mitigation. There is consensus that 120 will probably not show significant efficacy. Although we don't know what 240 will show, it presumably could be more effective than 120 and start to approximate 360."
Did I read that correctly?
A. Yes, you did.
Q. Do you recall that consensus in 2004?
A. I don't recall. Only what's written here.
Q. Further down in the memo, do you see "Arguments that Clinical Will Make," that heading?
A. Yes.
Q. And then does the memo identify four potential positions

that the commercial group thought clinical would espouse in relation to the discussion about dosing for Phase 2 MS BG-12?
A. I can confirm that there's four items listed below that statement, yes.
Q. And then your team prepared four responses to those potential positions?
A. My team. I can't confirm who prepared it or not, whether me, my team, or a group. But it appears as though the responses were prepared, correct.
Q. And one of the positions you thought the clinical team would make was that, at Number 3, the 120 arm that commercial is proposing may look like Biogen is trying to find a dose that doesn't work.
Is that correct?
A. That's what the sentence says.
Q. And then another concern that the commercial group thought the clinical team may espouse is that at, Point 4, what the commercial group is proposing only has one BID dosing arm.
Isn't BID important? Is that another potential position you thought the clinical team would have?
A. According to this memo, it was identified as a position -- as an argument that the clinical team will make.
Q. And then the first argument that you thought the clinical team may make is that "Option 1 is scientifically the best approach as it looks at different doses and frequency."

Is that correct?
A. According to the memo, yes.
Q. Returning back to the commercial rationale for Option 2, under the first bullet you indicate that "Commercial's first choice would be Option 4, which has a dosing arm of 1080" -- excuse me -- "1,080 milligrams, but there were safety concerns that would prevent that dose from being used in the study"?
A. That's what the sentence says, yes.
Q. I've handed you a document previously labeled as Bozic Exhibit 2, Bates-labeled BiogenM70012370-2371.
A. Okay.
Q. Is this -- are these meeting minutes prepared following a clinical trial review board meeting held February 19, 2004?
A. I can only confirm what the title says, "Clinical Trial Review Board Meeting Agenda Item, Meeting Minutes," yes.
Q. Was it a common practice for bodies such as the CTRB to prepare meeting minutes following a meeting by that body at Biogen?
A. I believe so.
Q. And do you recall seeing this type of document before?
A. I don't recall specific documents, seeing them, but I recall having seen, after meetings at Biogen and in different governance forms, the minutes.
Q. If we could look at the recipients -- or excuse me -- the attendees, list of attendees in the "others" category, can you

identify anyone beside yourself and John Oram who were involved on the commercial side?
A. Hans Peter Hasler, Bob Hamm, Sven Lee. I think those are the -- the only names that I recognize as having a commercial affiliation.
Q. Is the focus of this meeting the design of the Phase 2 study for BG-12 MS?
A. I cannot -- just whatever -- the agenda item is -- seems to state what the meeting was about. I don't recall this specific meeting to be able to accurately state what the meeting was, other than the item as listed.
Q. And the agenda item is "Double-blind placebo-controlled dose determination, efficacy, safety, and tolerability study of BG-12 in patients with relapsing-remitting MS."
Is that correct?
A. Correct.
Q. And under the list of attendees, there are people from a number of different functional groups; is that correct?
A. Yes.
Q. Including the CTRB chairperson, Carmen Bozic; is that correct?
A. That is correct.
Q. The clinical project manager, Rebecca Conaghan; is that correct?
A. Correct.

Q. The medical director, Gilmore O'Neill, was present; is that correct?
A. Correct.
Q. And the senior vice president of medical research, Whaijen Soo, was present; is that correct?
A. Yes, according to the document.
Q. And on the back of this page, is there a summary of the discussion at the CTRB meeting provided?
A. It's titled "Summarized Discussion," yes.
Q. And, again, we see a listing of four dosing options or dosing regimens -- sorry -- dosing regimes provided; is that correct?
A. Appears to be four options here, yes.
Q. And of these, Option 4, which included the 1080-milligram-per-day dose, had been discarded by the group; is that correct?
A. According to the sentence below the table that says "Option 4 was discarded," yes.
Q. And then the next paragraph or bullet indicates that "Dosing emerged as the most critical issue." Is that correct?
A. That's what it states, yes.
Q. And Option 2 appeared confusing to some of the CTRB members, correct?
A. According to the minutes, yes.
Q. Do you know why it was confusing to some people?

A. I do not.
Q. And then the next sentence indicates that "Commercial representatives were not in favor of a 240-milligram dose because this dose might affect the marketing strategy of the 720-milligram dose under development for psoriasis."
Is that correct?
A. Yes, according to the summary document.
Q. Does this refresh your recollection of potential concerns held by the commercial group about the revenue implications of a lower dose being used in the commercial product for MS relative to the dosing being used for psoriasis?
A. Give me a moment to read it, please. I can't recall the -- I can't recall the commercial opinion driving the -- the specifics of driving the commercial opinion.
Q. Under the summarized action plan, do the meeting minutes indicate that a concept was not approved at the meeting?
A. Correct.
Q. And so everyone was going to circle the wagons and try and find alignment on this issue?
A. All I can state is what is written here. "The team was instructed to seek alignment amongst the different interests and reconvene."
Q. And that sentence indicates that the parties that were primarily in disagreement were research and commercial; is that correct?

A. That's what it would seem to indicate.
Q. I've just handed you Sibold Exhibit 5, bearing Bates BiogenM10149900, which is an email from you to John Oram, dated June 13, 2004; is that correct?
A. Yes.
Q. And there's also a preceding email that John had sent to you on June 11, 2004; is that correct?
A. Correct.
Q. Going down to the last paragraph in John's email to you, does he provide some thoughts about dosing strategy for the study for BG-12 and MS?
A. He appears to offer some thoughts, yes.
Q. And does he explain that he was thinking you should not insert a 240-milligram BID or 480-daily-dose arm in the MS study?
A. So reading his note here, starting with, "given that we're trying to," it goes to, I'm thinking, maybe we should not insert a 240-milligram BID, 480-daily-dose arm in the MS study. Yes, that appears to be his thought, yeah.
Q. And that was his thought as a way to help differentiate the indications of MS and psoriasis?
A. I'm uncertain. I only have what -- I mean, he states at the end "just a thought." I'm not certain what he was basing this on other than what's in this email.
Q. He starts off by saying "Given that we're trying to

differentiate the two indications as much as possible," correct?
A. Correct.
Q. And then he proposes that Biogen not insert a 240-milligram BID arm in the MS study, correct?
A. Correct.
Q. And then he says "Would rather try to make it more likely that 720 will be the ultimate dose in MS," correct?
A. Correct.
Q. Just handed you Sibold Exhibit 10.
Is this an email that you sent -- or is the most recent email one that you sent on July 19 to John Oram?
A. Yes.
Q. It looks like the group is still debating what doses to use for the Phase 2 study for BG-12 MS?
A. Yeah, it appears that way on the memo.
Q. And on page 110 --
A. Yes.
Q. -- there's a heading, "Why bring this up?"
Do you see that?
A. I do.
Q. And then in the next paragraph, does it suggest that the group should reconsider whether to add BID dosing to the MS Phase 2 study because it was going to be investigated in psoriasis now?

A. I can only read what's in that paragraph and what that paragraph says, confirmed.
Q. I'll just read the paragraph.
"While the BG-12 MS CDT and SMT believed this issue had been resolved for MS back in February, it was pointed out that at that time BID dosing was not considered commercially important to investigate until after the U.S.A./E.U. psoriasis filing. Since that has changed, we are now being asked to reexamine BID in MS."
Is that correct?
A. That's what this sentence -- or the paragraph says, yes.
Q. And then later on, there are some things to consider for discussion that are provided by Cara; is that correct?
A. Some things, yes, correct.
Q. And she identifies a pro for adding BID dosing to C1900 as "If we are investigating BID in psoriasis during Phase 3, it is likely we will be asked at the BG-12 MS EOP2 why we did not look at BID in MS."
Is that correct?
A. As stated in the memo, yes.
Q. Does this refresh your recollection whether the EOP2 meeting is an FDA meeting?
A. It could be. I mean, as -- since the last, I'm thinking about what could that stand for. End of Phase 2, I'm assuming. I'm assuming that could be either an internal meeting or it

could be an FDA meeting. I can't speculate from the memo other than what's written here.

Q. And then she goes on to state that "Phase 3 is not a good place to look at two different doses given the number of patients we already may need to achieve our end points."

Is that correct?

A. Correct.

Q. Then if you could turn to page 108, the first page on this document. It looks like Sven Lee sent you an email on July 19.

Do you see that?

A. I see that, yes.

Q. And in the middle paragraph -- actually, in the first paragraph, does Sven indicate that Gilmore O'Neill had given him a call to see if it was still possible to add BID dosing to MS?

A. He states in the email "Gilmore called me to ask again if the BID issue was still open."

Q. And, apparently, Whaijen had asked Gilmore about that again?

A. Yes, next sentence.

Q. And then in the next paragraph, Sven states that at this point he thinks Biogen should proceed with TID, or three times daily dosing, for MS.

Is that correct?

A. Correct.

Q. Do you think that's a reasonable interpretation of what Sven states?

A. I can't speculate.

Q. And Sven goes on to state that "With MS patients will be more willing to stay on a TID, or three times daily, because they can't 'see' their disease."

Is that correct?

A. That's what he says, yes.

Q. Then he goes on to acknowledge that "TID is not very convenient for chronic therapy."

Is that correct?

A. Correct.

Q. You've just been handed a document previously identified -- or marked as Bozic Exhibit 10, bearing Bates M10158120-122 --

A. Okay.

Q. -- with the most recent email being from David Allsop to a number of individuals, including yourself, on July 28, 2004.

Is that correct?

A. Yes.

Q. And the subject is "Draft commercial slides for BG-12 MC meeting"?

A. Uh-huh. Yes.

Q. Do you remember if MC is management committee?

A. I don't recall.

Looking on the next page, though, it says "Preparation for

BG-12 management committee." So, yes, I would say MC is management committee. Sorry.

Q. Then there's a reference to Dan.

Do you know who Dan is?

A. Yes. Dan Koerwer.

So during this time I was transitioning to Australia, and Dan was backfilling me in the new products commercialization role. So I officially began in -- at the beginning of August somewhere, and I was on vacation during that time as well, I recall.

Q. So when it says "Dan's team," that was previously your team?

A. Correct.

Q. So Dan's team, Bob Hamm, and David Allsop had a brief conversation -- or brief conference call prior to the CRB meeting; is that correct?

A. Looking at this email, that's what he's stating -- that's what David is stating.

Q. According to this email, that group made the decision, based on the delay and danger of a sub-720 dose in MS pulling down the price to an unacceptable level. They made the decision not to do a 480-milligram dose.

Is that correct?

A. Well, he says that the CRB decided not to do the 480-milligram, and then down below states that they'd had the

call. We made that decision based on the delay and danger as you had read.

Yeah, I can only confirm exactly what's written here and can't speculate or fill in. I wasn't -- as you can tell by this, wasn't at the meeting. Don't know what was said. I'm not sure. I can confirm what's in the email and assume that that's what the reasoning was, but I don't know the thinking behind it.

Q. In that email there's an indication that there's a danger a sub-720 dose in MS would pull down the price to an unacceptable level.

Do you see that?

A. I do.

Q. Do you know why a sub-720 dose in MS would pull down the price to an unacceptable level?

A. I'm not sure of the details other than in previous documents you showed that there were comments about psoriasis. So that's what it appears to be referring to.

Q. Referring to the fact that, if you have a dose lower than 720 for MS and a dose of 720 for psoriasis, that would pose problems because you'd have to reduce the price an unacceptable level; is that correct?

A. A lot of dots connected there. I think that what they are saying specifically in this email is that, if it were below 720, then it would bring down the MS price to an unacceptable

level. So that's what David believed in this message or seems to be communicating.

Q. Today we've looked at a number of documents containing statements about the implications of the dosing for MS relative to the dosing for psoriasis on pricing of those products.

Would you agree?

A. I believe so. I'd have to go back and look at the documents. Again, I'm looking at these for the first time in a very long time, and they're not familiar, the documents. But there was reference to dosing and different indications, yes.

Q. And the commercial preference, as reflected in all of those documents, was that a higher dose or at least the same dose be the one chosen for MS as psoriasis?

A. It was pointed out the difference, potential differences in dosing. And here it clearly states the danger of a sub-720 dose in MS pulling down the price to an unacceptable level.

Q. And following the recommendation, which was based in part on that concern, the CRB decided not to test 480 milligrams in the Phase 2 study for MS; is that correct?

A. Here it states the CRB decided to not do the 480 milligrams because it would delay the MS study by at least six months and this would take the initial results well past Germany launch.

So, according to this, that was the basis of the CRB decision. But I don't have enough information to be able to state beyond what's written here.

Q. And the next sentence says that the CRB decision was on recommendation from commercial, correct?
A. It says "This was on recommendation from commercial."
Q. I've handed you Sibold Exhibit 11, bearing Bates BiogenM10124968-978. This is a Biogen Idec slide deck dated September 27, 2005, entitled "BG-12 MS Go/No-Go Discussion."
I'm just going to ask questions on one page, but feel free to skim through it. The page I'm going to ask about is 975.
A. Okay.
Q. On this page is Biogen game-planning how to address the possibility that the dose for MS will be below 720 milligrams?
A. I can't answer the question. I am not familiar with this deck, and I lost touch with that program as of August 2004 when I went to Australia.
Q. Do you see the heading is "If clinical trials indicate a starting dose other than 720 milligrams, it will be very difficult to ensure sufficient revenue for commercial viability"?
A. I see that, yes.
Q. And then below that there is a decision tree, correct?
A. Yes, it appears to be so.
Q. And the initial question is "Does 120 or 360-milligram dosing have similar efficacy to 720 milligrams with improved safety/tolerability?"
Do you see that?

A. I do.
Q. And if the answer is no, then the decision tree indicates the answer would be "Price at psoriasis price per cap."
Do you see that?
A. Yes.
Q. And cap to be capsule?
A. Not sure, actually, because it's per capsule, and that price below does not seem, to me, to correlate to an annual. So I'm just not certain. I, again, am not familiar with this document or the terminology that the team was using.
Q. And then if the answer is yes, does the decision tree lay out three possible approaches for addressing the possibility that a dose of 120 or 360 would have similar efficacy to 720?
A. All I can surmise from this is what's written here, "Is full psoriasis clinical development being undertaken?" Yes, yes, and no. And the detail is below that.
Q. One of the options is two brands, two prices.
Do you see that?
A. That's what it says, yes.
Q. And that's explained as being the creation of two brands to be launched with different names, formulations, and prices for psoriasis and MS; is that right?
A. I'm not sure it states psoriasis and MS, but create two brands to be launched with different names, formulations, and prices in separate markets -- in the separate markets.

And I don't know whether markets is referring to indications or geographies.

Q. Given the context, don't you believe it's indications?

A. I can't speculate. I can't speculate. I'm not going to speculate. Again, there's clearly a lot of work done behind this document. I'm not familiar with it, don't know what the team was thinking, was no longer involved with the program. So I really -- I don't know.

Q. Okay. The next option says "Price out of psoriasis. Give up significant psoriasis business by superoptimally pricing for that market to gain revenues in MS."

Do you see that?

A. I do.

Q. And then the third possibility is that there just wouldn't be a psoriasis launch; is that correct?

A. It appears from this document, yes.

Q. Did your group consider these same options while you were involved with the BG-12 MS clinical development plan?

A. I don't recall.

Q. No recollection?

A. No recollection of considering the options here.

Q. Based on your experience, do you have an understanding of why it would have been problematic for Biogen, from a revenue or pricing standpoint, if the dose used to treat MS was below the dose used to treat psoriasis?

A. Differential -- different -- whenever you have a product, this is kind of something that was part of the new products team is, as we looked at multiple indications for products, you would consider the implications of how do you have different indications with the same product.

And one of the considerations would be is there a price differential? Just the complexity that having different indications creates.

Q. Why would -- the fact that a lower dose would be used for MS than psoriasis, why would that in practice affect the pricing for the two different indications?

A. Well, practically, if you had one dose for one indication and another dose for another indication, and if it was either higher or lower, it would have implications based on whatever you set your pricing for the first indication.

So if there's different doses for different indications, you know, it adds, as I said, complexity.

Q. So is it fair to say that, if the capsule price was the same for both indications, you would make less money on MS if the daily dose was lower for MS than psoriasis?

A. Potentially, but not with certainty, because there's other variables involved and the capabilities of the system, et cetera.

Q. And would you agree that it was that consideration that resulted in the -- that was one consideration that resulted in

the commercial team having a preference for a higher dose rather than a lower dose in the clinical studies for MS?
A. I'm sure it was a consideration, one of many considerations when putting forth a program. Ultimately, though, the development program is determined by the clinical development team and the governance surrounding that.
Q. But you were not involved in that decision in the case of BG-12 MS; is that correct? The ultimate decision?
A. In which decision?
Q. The ultimate decision for the Phase 2 dosing for BG-12 MS.
A. I don't believe that I was on any of the governance committees, because I believe they were all within the R&D function that were the decision makers on those committees.

But I would have to -- I can't recall the committees that I sat on or didn't or where I had a vote on or was just a participant. But I personally did not make any decision regarding the final outcome for this or any other program at Biogen.

MS. BLOODWORTH: Thank you, Your Honor. That concludes that testimony. We have one more ready to play. It runs 59 minutes.

THE COURT: That should be fine.

MS. BLOODWORTH: Okay. Thank you, Your Honor.

Ms. Greb will also introduce the witness.

THE COURT: Thank you.

MS. GREB: Your Honor, the next witness that Mylan will call is Dr. Carmen Bozic by video designation. We've also prepared some binders for that designation as well.

THE COURT: All right. Thank you.

MS. GREB: Dr. Bozic was a senior medical director at Biogen. She served as a chairperson on the Biogen clinical trial review board and was responsible for the approval of clinical trial protocols. She was also at the end of Phase 2 meeting with the FDA. Dr. Bozic will testify about the clinical trial protocols and the discussions regarding the Phase 2 and Phase 3 trial.

For the record, the exhibits that will be referenced during the testimony of Dr. Bozic are Exhibit 1C, which is JTX 2035; Bozic Exhibit 1D, which is JTX 2036; Bozic Exhibit 1F, which is DTX 1489; Bozic Exhibit 2, which is JTX 2039; Bozic Exhibit 3, which is JTX 2040; Bozic Exhibit 8, which is JTX 2144; Bozic Exhibit 13, which is DTX 1527; and Bozic Exhibit 18, which is JTX 2044.

Thank you.

THE COURT: Thank you.

(Video played and reported as follows.)

Q. Can you please state your name for the record.

A. Carmen Bozic.

Q. And, Dr. Bozic, you're a medical doctor, correct?

A. Yes.

Q. Then you have experience working on several drugs related to multiple sclerosis, correct?
A. Yes.
Q. And was this work all done as an employee of Biogen?
A. Yes.
Q. And you started at Biogen in 1998, correct?
A. Yes.
Q. What was your role when you started in 1998?
A. I was an associate medical director.
Q. And what were your responsibilities as an associate medical director?
A. I was responsible for designing and overseeing clinical development plans and clinical trials.
Q. And how long were you in that role?
A. I was an associate medical director for approximately three years.
Q. And what was your next role at Biogen?
A. I was medical director.
Q. Okay. And how did your responsibilities change?
A. I had the same responsibilities.
Q. And how long were you in that role?
A. Two years.
Q. Two years. So that's 2001 to 2003?
A. Yes.
Q. And then how about after that?

A. Then I was senior medical director.
Q. And did you have the same responsibilities as senior medical director?
A. Yes.
Q. And how long were you in that role?
A. About two years.
Q. Two years. Okay.
And how about after that?
A. Then I became senior medical director of clinical trial safety.
Q. And what were your responsibilities in that role?
A. I oversaw the safety of subjects enrolled in our clinical trials and in our approved products.
Q. And how long were you in that role for?
A. Until early 2005. Until the fall of 2005.
Q. Okay. And then what did you do?
A. I'm sorry. I was there from early 2005 until early 2006 in that role.
Q. Okay. And then after being senior medical director of clinical trial safety, what role did you take on?
A. Then I became the head of safety at Biogen in early 2006.
Q. And did your responsibilities stay the same as head of safety?
A. No.
Q. How did they change?

A. They expanded to include the safety of our patients in clinical trials and postmarketing as well as safety operations.
Q. What does "safety operations" mean?
A. It means the management of adverse events that we receive on our products during development and in the postapproval space.
Q. Okay. And how long did you do that for?
A. I was the head of safety from early 2006 until the summer of 2013.
Q. Okay. And what was your next role?
A. In the summer of 2013, I became the head of clinical and safety sciences.
Q. And what responsibilities did you have as head of clinical and safety --
A. Sciences.
I oversaw human safety, preclinical safety, as well as clinical development across our therapeutic areas.
Q. And how long were you in that role for?
A. I was in that role from summer of 2013 until April 2015.
Q. And what did you do after that?
A. Then I became the head of global development.
Q. And what were your responsibilities as head of global development?
A. For the first six months, I oversaw clinical development across our late-stage therapeutic areas, as well as safety,

clinical operations, and biometrics.

Q. And are you still in that role today?

A. No.

Q. So what did you do after becoming head of global development?

A. In the fall of 2015, my role continued to be called head of global development, but the responsibilities changed.

I was now accountable for human safety, regulatory affairs, clinical operations, biometrics, R&D compliance, medical writing, as well as Japan development.

I also had accountability for Japan development starting in the summer of 2014.

Q. Okay. And what was your next position at Biogen?

A. In September of 2017, I became the head of the portfolio transformation, also called portfolio transformation leader.

Q. And what are your responsibilities in that role?

A. In this role, I oversee ways in which we can increase the size, speed, and probability of success of our portfolio.

Q. When did you start working on the BG-12 program?

A. I started working on the BG-12 program in February of 2004.

Q. Okay. And so, at that time, you were senior medical director; is that correct?

A. Yes.

Q. And what was your involvement on the BG-12 MS program in February of 2004?

A. I was the chairperson of the clinical trial review board.
Q. And what is the clinical trial review board?
A. It's a board that oversees our protocol concepts for molecules in development and molecules that are approved and where we're continuing to do development.
Q. And is the clinical trial review board also referred to as the CTRB?
A. Yes.
Q. The CTRB operated or provided guidance with respect to other development programs at Biogen?
A. The CTRB reviewed many development programs at Biogen.
Q. And during your time as chairperson of the CTRB, how many other drug development projects did you oversee?
A. That would be very hard to estimate.
Q. Would it be more than 10?
A. Yes.
Q. More than 20?
A. Yes.
Q. And what were your responsibilities as chairperson?
A. I chaired the CTRB meetings where the protocol concepts were reviewed.
Q. And who had decision-making authority on the CTRB?
A. I approved the protocol concepts, and I signed off on the final protocols.
Q. And were there other members on the CTRB, other board

members?
A. Yes.
Q. Did the board have to reach a consensus to make a decision?
A. We listened to many different voices on the board in order to make a decision.
Q. I would like you to turn to Exhibit 1C, please.
Have you seen this document before?
A. Yes.
Q. And what is this document?
A. These are the slides that were presented at the February 19th, 2004, CTRB meeting.
Q. So did Dr. O'Neill present these slides?
A. Yes.
Q. So the second point lists -- or states "Dosing is only possible in multiples of 120 milligrams."
Do you see that?
A. Yes.
Q. How is this a constraint on the BG-12 MS program?
A. That was the size of the capsules that we had at the time.
Q. So Biogen couldn't test, for example, a dose of 500 milligrams per day or 400 milligrams per day, right?
A. We could have, but we would have to reformulate into different-sized capsules.
Q. And the fifth bullet point down says "Psoriasis dose already established at 720 milligrams."

Do you see that?

A. Yes.

Q. How was the established dose of 720 milligrams of BG-12 for psoriasis a constraint on the BG-12 MS program?

A. The highest dose tested in the psoriasis studies at that point in time was 720 milligrams.

Q. And so how was the testing of the highest dose in the psoriasis program a constraint on the BG-12 MS program?

A. It means that was the maximal dose that had been shown to be safe at that point in time in psoriasis patients.

Q. And the next bullet point down says "Regulatory - adequate dose determination is a requirement."

Do you see that?

A. Yes.

Q. What does that mean?

A. It means that the regulators expect different doses to be evaluated.

Q. And can you turn to the page ending in Bates Number 12333.

What is this slide showing?

A. This is a summary of dosing options for the Phase 2b study of BG-12 in MS.

Q. And who devised the four dosing options?

A. It would have been Gilmore O'Neill.

Q. Okay. And what makes you say that it would have been Dr. O'Neill?

A. He was representing the entire clinical development team.
Q. And Option 1 and Option 2 are the only two that include a 480-milligram-per-day dose, correct?
A. Yes.
Q. And these two dosing options were discussed but eventually rejected for the Phase 2 clinical trials, correct?
A. The options were discussed. And eventually, Option 3 was selected as the option to go forward with.
Q. So the 480-milligram-per-day dose was not tested in the Phase 2b clinical trials, correct?
A. No.
Q. And no BID dosing was tested, correct?
A. That's correct.
Q. Can you turn to page ending in Bates Number 12335.
And the title to this slide says "Lead Option, Option 1 treatment schedule."
Do you see that?
A. Yes.
Q. And so this says "Placebo BG-12, 120 milligram BID," which would be 240 milligrams per day. "BG-12, 120 milligrams TID," which would be 360 milligrams per day. "BG-12, 240 milligrams BID," which would be 480 milligrams per day. And "BG-12, 240 milligrams TID," which would be 720 milligrams per day.
Correct?
A. Yes.

Q. Why was this called the lead option?
A. This was the preferred option by Dr. Gilmore O'Neill.
Q. And so you stated before that Dr. O'Neill was presenting on behalf of the clinical group, correct?
A. Yes.
Q. So is this the lead option for the clinical group or just Dr. O'Neill?
A. He was the leader of the group. So what I do know is that it was his lead option.
Q. So he didn't state during the presentation why it was his lead option?
A. On page 20 it provides some evaluation of Option 1.
Q. And that's the slide titled "Critique of Option 1 Concept," correct?
A. Yes.
Q. And then there's a bullet point that says "Commercial." And underneath, it says, "Endorses Option 2."
Do you see that?
A. Yes.
Q. So is this stating that the commercial group did not endorse Option 1?
A. It just says that commercial endorses Option 2.
Q. And what do you understand that to mean?
A. It means that commercial approved, liked, Option 2.
Q. But not Option 1?

A. I mean, it's implied.

Q. And let's turn to the page ending in Bates Number 12340, which is the next page.

A. Uh-huh.

Q. And this says at the top, "Option 2 Treatment Schedule."

Do you see that?

A. Yes.

Q. And under the first bullet point, then there's the second subbullet point down, and the dosing for Option 2 is listed as "Placebo, BG-12, 120 milligram QD," which is once daily. "BG-12, 120 milligrams TID," which is three times daily. "BG-12, 240 milligrams BID," which is twice daily. And "BG-12, 240 milligrams TID," which is three times daily.

Do you see that?

A. Yes.

Q. And then under "Commercial," it says "prefers this option."

Do you see that?

A. Yes.

Q. And then if you turn to the next page, the slide is titled "Option 3 Treatment Schedule."

Do you see that?

A. Yes.

Q. And then under the first bullet point, in the second subbullet point, it shows the dosing for Option 3. And this is "Placebo, BG-12, 120 milligram QD," or once daily. "BG-12, 120

milligrams TID," which is three times daily. And "BG-12 240, milligrams TID," which is three times daily.

Do you see that?

A. Yes.

Q. And Option 3 is the option that was eventually selected, correct?

A. Yes.

Q. So you said that Gilmore thought that. This bullet point from regulatory, that came from Dr. O'Neill, not the regulatory group?

A. He was the one presenting.

Q. And then underneath, it says "Commercial," and then "preferred over Option 1."

So this is saying that commercial preferred Option 3 over Option 1, which was the lead option for the clinical group; is that correct?

A. Yes. But remember they also endorsed Option 2 as well.

Q. And I'd like to introduce as Exhibit 2 a document Bates-labeled BIOGEN F70012370 to 371. And what is it?

A. It's the meeting minutes for the CTRB meeting held on February 19, 2004.

Q. And looking down at the list of attendees under "Others," can you tell me who Hans Peter Hasler is?

A. He was a commercial person.

Q. What about Bill Sibold?

A. He was from the commercial organization.
Q. And what about Bob Hamm?
A. He was from commercial.
Q. If you can turn to the second page, please.
So the chart on the second page, are these the same dosing options as presented by Dr. O'Neill?
A. Yes.
Q. And underneath, it states under the first bullet point, "Dosing emerged as the most critical issue."
Why was it the most critical issue?
A. Generally in a Phase 2 study, dosing is a very important issue.
Q. And why is it a very important issue?
A. Because it's your opportunity to establish the efficacy and safety of a range of doses.
Q. And then it says "Option 2 appeared confusing to some CTRB members."
A. Yes. I see that.
Q. Do you see that?
Okay. Option 2 was commercial's preferred option, correct?
A. Commercial endorsed Option 2, and they preferred Option 3 over Option 1.
Q. And so what kind of potential pricing issues were they concerned about?
A. I don't know the details.

Q. And then in the bottom -- sorry -- the third bullet point down underneath the chart, it says "BID dosing was discussed, and it was thought that this dosing regimen was beneficial on many different levels."

Do you see that?

A. Yes.

Q. Why was BID dosing considered to be beneficial?

A. Gilmore was very -- felt very strongly that BID dosing should be evaluated in the Phase 2b study. MS is a chronic disease. Patients have to take their treatments for many years. And so developing a BID dosing could help ensure better compliance in that setting.

Q. So, Dr. Bozic, just before we begin, are you able to tell us what considerations were involved in the dose selection without looking at your declaration?

A. Yes, I can, but I'd like to be as accurate as possible by referring to my declaration.

Q. Okay. Go ahead.

A. So one of the considerations was that a dose -- one of the considerations was that a study with three active dosing arms would be considered a true dose-ranging study.

A typical dose-ranging study in Phase 2 has three active dosing arms: a low dose, a mid dose, and a high dose. So that was a point in favor of Option 3.

Limiting the trial to three active dose arms, which is

typical in a Phase 2b trial, aligned with our goals to promptly commence and complete the study and to advance the program.

Adding a fourth active dosing arm would require a greater number of total patients and would lengthen the time to conduct the study.

The 240-milligram TID dose made sense to the CTRB because it had already been tested in psoriasis patients and it was the highest dose tested in psoriasis patients. It was shown to be safe.

The CTRB also supported the 120-milligram QD dose as the lowest dose because that would potentially be a minimally effective dose in a dose-ranging study.

And then, regarding the third dose, the CTRB favored 120 milligrams TID, or 360 milligrams per day, because it would maintain consistency with the three-times-per-day dosing regimen of the high dose at 240 milligrams PO TID.

It would have been difficult to vary both the dose and the dose frequency and maintain a reasonably sized and rapidly feasible three -- dose-ranging study.

Q. Okay.

A. For example, if you were to include all the potential doses and all the potential dosing frequencies, you would have six active dose arms. And that's a bigger study and much more difficult to conduct.

By having a three active dose -- a three-active-arm

proposal in Option 3 would result in more patients enrolled in each dosing arm and would increase the statistical power of the study compared to a four-active-arm proposal.

So those were the many considerations that went into the ultimate choice of doses for the Phase 2b study of BG-12 in MS.

Q. Just a couple questions about that.

So you stated that one of the goals of the program was to start the clinical trial right away?

A. Our goal was to start it as rapidly as possible.

Q. So you don't recall whether or not she said there would be a delay from adding another dosing arm?

A. I don't recall that -- a discussion around that.

Q. And you also said one of the factors was the difficulty in having a variety of dosing sizes and dosing frequencies in the clinical trials; is that correct?

A. Yes. And the reason is we didn't know what was driving the efficacy of BG-12.

Q. So Dr. O'Neill was the medical director for the BG-12 program, correct?

A. Yes.

Q. And so was he the one that was designing the clinical trials?

A. Yes.

Q. Right. So he proposed options that involved both BID dosing and TID dosing. So my question to you is, if it was

difficult to have different dosing sizes and dosing frequencies -- as you said, this was a factor -- why would Dr. O'Neill propose that?

A. He believed that 240 milligrams BID should be evaluated in the study. That was very important to him.

Q. And what makes you say it was very important to him?

A. Because he presented it as the lead option, and he also spoke to me around that time that he thought 240 milligrams BID should be tested in MS patients.

Q. The second page, the bottom bullet point. So "The concept was not approved. The team was instructed to seek alignment amongst the different interests -- i.e., research and commercial -- and reconvene an ad hoc CTRB as soon as possible, preferably the week of February 23rd, with an updated and agreed-upon study design."

So is this stating that there was not alignment between research and commercial?

A. It says the concept was not approved at the CTRB meeting on February 19, 2004.

Q. So there wasn't alignment between research and commercial?

A. That's what it says. There were many voices at the CTRB, many different perspectives.

Q. And do you recall why there wasn't alignment?

A. I mean, commercial preferred Option 2 and also supported Option 3 over Option 1. Gilmore O'Neill, on the other hand,

thought the lead option should be Option 1.
Q. And so the dosing that was being discussed at the CTRB, this was relating to the protocol concepts, correct?
A. The protocol concept for the Phase 2b study of BG-12 in MS, yes.
Q. Okay. And so dosing was a key component of the protocol concepts, correct?
A. Dosing is always included as a point in the protocol concept.
Q. You said dosing was always included as a point in the protocol concept, correct?
A. Yes.
Q. Why was dosing always part of the protocol concept?
A. It's an important part of the study design considerations.
Q. And why is it an important part?
A. As part of drug development, it's important to find the right dose that's safe and effective.
Q. So if Biogen had -- in 2004, if Biogen had intended to market a specific dose, it would have included that dose in its Phase 2b trials, correct?
A. Not necessarily. The important thing is to establish a dose range where you have safety and where you may have efficacy, and that gives you flexibility to continue to evaluate additional doses further on in Phase 3, for example.
Q. Okay. And so in the dose range, if the dose that Biogen

wanted to market fell within that range, couldn't it still have a dose-ranging study by including that dose?
A. Can you rephrase that, please?
Q. Sure.
A. Clarify that.
Q. You said that it's important to establish a dose range for a Phase 2b study, correct?
A. Yes. It's important to test a range of doses in the Phase 2b studies.
Q. Right. So if Biogen had a specific dose in mind that it wanted to market for what eventually became Tecfidera, couldn't it be included as part of that dose-ranging study?
A. It could be included, but it doesn't have to be included, because you always have the option to include it subsequently.
Q. So Phase 2b tested efficacy as well as safety, correct?
A. Yes.
Q. But if Biogen had a specific dose in mind in February 2004, testing that dose in the dose-ranging study would have provided it more information on efficacy and safety, correct?
A. We didn't know what was going to be effective in MS when we were designing the Phase 2 study, and we had a lot of different options to consider. There were also a lot of different doses to consider. So all that went into then the final set of doses that were tested in Phase 2.
Q. And the commercial people and the regulatory people and the

clinical people, they were all involved in the dosing decision, correct?
A. There were many voices at the CTRB and subsequently that were involved in the dosing decision.
Q. Okay. So you stated that the ad hoc CTRB meeting mentioned in the meeting minutes was not held, correct?
A. That's correct.
Q. And why was it not held?
A. I received an email from Al Sandrock subsequently.
Can we pull that up as an exhibit?
Q. For the record, this is document Bates-labeled BiogenF10157897.
So this is an email from Alfred Sandrock dated February 27, 2004. Do you see that?
A. Yes.
Q. Who is Alfred Sandrock?
A. He was the head of the neurology clinical development team at the time.
Q. Would he have been Gilmore O'Neill's boss?
A. Yes.
Q. So it states "After many discussions between Gilmore and Bill over the past week and after discussions today with Whaijen and Burt, it was decided that Option 3 is the design of choice for the Phase 2b trial in MS."
So who is Bill?

A. Bill Sibold was a commercial representative.
Q. And who is Burt?
A. Burt Adelman was the head of research and development.
Q. So Mr. Sandrock is saying that he discussed dosing with Dr. O'Neill, someone from commercial, the head of R&D, and then the head of medical research; is that correct?
A. He alludes to many discussions between Gilmore and Bill and discussions with Whaijen and Burt.
Q. So then commercial personnel were involved in the discussions that ultimately led to the choice for Option 3, correct?
A. Based on this email, Bill Sibold was involved.
Q. Do you know what they discussed?
A. I wasn't part of the discussions.
Q. I would like to introduce as Exhibit 3 a document Bates-labeled BiogenF10156888 to 889.
Have you seen this document before?
A. No.
Q. Do you know what it is?
A. The document says that it's CDT meeting discussion minutes, dated December 18, 2003.
Q. And were meeting minutes like this kept in the ordinary course of Biogen's business?
A. Yes.
Q. So looking under the second or the third note that starts

with "Action" --
A. Yes.
Q. -- two bullet points down from that, it says "Commercial would like a dose for MS that is different and not a multiple of the psoriasis dose. The issue there would be the current cost of Fumaderm will affect the costing for BG-12."
Do you see that?
A. Yes.
Q. So in order to answer, you'd have to speculate as to commercial's viewpoint regarding dosing?
A. What I do know is that -- based on my prior testimony, is that commercial was concerned about pricing considerations between psoriasis and MS, in particular, related to the 120 milligrams BID dose.
Q. So commercial's concerns were a factor considered in making the ultimate dosing decision for the Phase 2b trial, correct?
A. Commercial's perspective was one factor, but it was not the only factor.
Q. And how would the results of the MS phase 2 study impact the pricing of BG-12 psoriasis?
A. Commercial was concerned that the price in MS and psoriasis might affect each other. They might be related in some way.
Q. But wasn't pricing a factor considered in the choice of dose?
A. Commercial had a perspective. You know, they had input on

the fact that they had concerns that the dosing in MS and psoriasis may influence each other.

Q. So was commercial's involvement in the BG-12 program at this stage to provide advice relating to pricing?

A. Commercial provides input on a variety of commercial topics on programs.

Q. But --

A. Pricing is one of them.

Q. I'd like to mark as Exhibit 8 a document Bates-labeled BiogenF10158112 to 114.

Have you seen this document before?

A. Yes.

Q. And what is it?

A. It's an email between Carey Smith, who's an associate director of regulatory affairs, to Jennifer Jackson and Nadine Cohen, both of whom were more senior people in regulatory affairs. And Nadine Cohen was the head of regulatory affairs at the time.

Q. And this document is -- or this email -- excuse me -- is dated February 25, 2004?

A. Yes.

Q. And so this was after the CTRB meeting?

A. Yes.

Q. So the first paragraph there, Ms. Smith writes, "The CTRB last week for BG-12 MS Phase 2 study ended in a stalemate

between clinical/regulatory and commercial. The outstanding issue is what is the best study design to optimally study dose ranging."

Do you see that?

A. Yes.

Q. So the next paragraph she states, "Of options outlined in the minutes below, clinical and regulatory favor Option 1 while commercial favors Option 2 or 3." And then in brackets "We are limited by the fact that we only have 120-milligram capsule at this time. The argument for Option 1 is that, given all of the limitations, it represents the most scientifically sound design. However, commercial is concerned about using the 240-milligram dose and the potential impact on pricing for both psoriasis and MS."

Do you see that?

A. Yes.

Q. But Ms. Smith here is stating that clinical and regulatory favored Option 1?

A. Those are her words, yeah.

Q. And she also states that the Option 1 dosing regimen represented the most scientifically sound design.

Would you agree with that statement?

A. That was Gilmore's opinion at the time.

Q. And just for the record, Exhibit 1F is Bates-numbered BiogenF70012384 through 2389.

A. So this document includes the meeting minutes from a BG-12 MS CDT meeting that was held on July 5, 2006. And in these meeting minutes you can see on the final page that one of the action items was to calculate the additional patients needed if a 480-milligram dosing arm needs to be added to the Phase 3 protocols.

Q. Can I ask you, what does that mean where it says "calculate the additional patients needs if a 480-milligram dosing arm needs to be added to the Phase 3 protocols"?

What does it mean by "if it needs to be added"?

A. It meant that the team was considering adding 480 milligrams into the Phase 3 study.

Q. And they were considering this because they were anticipating questions from the FDA, correct?

A. Not necessarily. I mean, they were considering it because Gilmore continued to believe that 240 milligrams BID was an important dose to test in MS patients, and they were planning and preparing --

Q. Right, but we've --

A. -- for this dose.

Q. But we've looked at documents today where, around this time period, Biogen was anticipating questions from the FDA regarding BID dosing and why BID dosing wasn't included, correct?

A. Can you repeat your question.

Q. So we've looked at documents today where the BG-12 MS team was anticipating questions from the FDA regarding BID dosing, correct?
A. Yeah. All those documents were in the 2004 time frame at the time that the Phase 2b study was designed.
This refers to, once the data was known for the Phase 2b study, now you're planning for the Phase 3 study.
Q. And so if they anticipated questions about BID dosing for the Phase 2 study, you don't think they would anticipate questions regarding dosing for the Phase 3 study?
A. That's possible, but the team was already preparing and planning for the 480-milligram dose, as evidenced by these meeting minutes.
And then you can see on the cover of the document, the front page of the document, you can see that Minhua Yang, who was the statistician, was also calculating the sample size that would be needed for the inclusion of 480-milligram-dose arm into both Phase 3 studies.
Q. You said that they were preparing and planning for the addition of this dose, but it just says if it needs to be added, right? It wasn't saying it will be added?
A. Well, they hadn't made a final decision yet. But they were planning, you know, to -- you know, evaluating and preparing in case it was to be added.
Q. So then, other than this one document, do you have any

other documents that indicate that Biogen was considering the 480-milligram dose for the Phase 3 trials at this point in time?

A. I also recall speaking to Gilmore O'Neill at that time, and he thought it was very important to include the 240-milligram BID dose into the Phase 3s.

Q. And he had been thinking that previously for the Phase 2b trial too, correct?

A. That's correct.

Q. And Biogen did not follow his advice for the Phase 2b trial, correct?

A. There were many considerations in the Phase 2b study. We ended up with Option 3, but Biogen -- but Gilmore continued to believe that 240-milligrams BID should be evaluated in Phase 3.

Furthermore, the results of the Phase 2b study allowed us to study the 240 BID study in Phase 3 because, in that Phase 2b study in MS, we demonstrated that 720 milligrams per day was safe and effective in MS. We also showed that 360 milligrams per day, or the 120 TID dose, was safe but not statistically significant in MS.

So we had covered a range of doses that would then allow us in Phase 3 to test not only 720 milligrams per day but also the 480 milligrams per day.

Q. So the Phase 2b study didn't provide any new information on any of the doses regarding safety below 720 milligrams,

correct?
A. No. The study provided information on the safety of BG-12 in MS at the 720-milligram dose and at the 360-milligram dose and at the 120-milligram dose per day. So that was not known actually before running the Phase 2 study. And of course the efficacy of BG-12 in MS was also not known before running the study.
Q. Okay. Did Biogen think that 480 milligrams per day was likely to be effective, based on the Phase 2b study?
A. We didn't know that. We didn't know that.
Q. Dr. Bozic, do you have any documents, other than this one single document, to show that Biogen was considering the 480-milligram dose at this time?
A. I think this is the main document. We can go also to my declaration, if you want, to see kind of the rationale for --
Q. I'm curious if there are any contemporaneous documents from this time period, not from 2016 when I believe you wrote that declaration, but any documents from the 2006 time period that shows that Biogen was considering the 480-milligram dose.
A. Let me check through. This is the document.
Q. Are you aware of any documents suggesting that a 480-milligram dose should be tested in Phase 3 earlier than July 2006?
A. You know, in this exhibit there's also a reference to Minhua Yang completing a sample size estimate in June of 2006.

So it's at the front of the exhibit. So based on that, the team was already planning for the 240-milligram BID dose in June of 2006.

Q. You said the team was planning for the 480-milligram dose in June, but Ms. Yang's email, if you look on Bates page ending in 385 at the very top, it states "if 480-milligram arm is added."

So she's not saying it will be added; she's says if it is added.

A. Yes, it says if it was added, yes.

Q. And are you aware of any document earlier than June 2006 in which someone at Biogen was suggesting to test the 480-milligram dose in Phase 3?

A. No.

Q. The dose that you're proposing for the Phase 3 clinical trials?

A. Yeah. Remember too that, in these FDA meetings, we have a lot of questions that we have for the FDA, including the patient population, the clinical end points, as well as the dose. And there's a limited amount of time in which to have all those questions.

So we knew that, if we proposed the dose of 720 milligrams per day for the Phase 3 studies, we could always go back afterwards and include the 480-milligram dose.

So it was really not necessary to put forth a 480-milligram

dose to the FDA.
Q. But you asked them for approval, correct? Or we'll come back to that, but you asked them for approval on the 720-milligram dose for the Phase 3 trial?
A. We did because we knew, if they had their approval for 720 milligrams, we could always go back and put 480 milligrams into the protocol, because if 720 milligrams is acceptable to regulators from a safety perspective, then you can always test a lower dose.
Q. Okay. But, if you were planning at that time to include both the 480-milligram dose and the 720-milligram dose, why wouldn't you just ask for both?
A. The reason is that you want to limit the amount of questions that you put forth in front of the FDA, hold to those questions that are absolutely essential to get their input on. And we had questions on clinical end points. We had questions on patient population. And, of course, we wanted to make sure that they agreed with the top dose that we would include into the Phase 3. It was simply not necessary to discuss the 480-milligram dose with the FDA at the time given the limited amount of time that you can have with them.
Q. Are you aware of any documents that Biogen has that show any discussion among Biogen employees about not discussing the 480-milligram dose with the FDA because it wasn't necessary?
A. No.

Q. Who prepared this document?
A. Many people worked on this document. You know, the regulatory team, medical writing, and different functions would be submitting different parts -- would be providing different parts of the document.
Q. And what's the purpose of the end of Phase 2 information package?
A. It's to provide the FDA with the Phase 2 data as well as a summary of all the available data on the molecule to date and to ask the FDA questions around the design of the Phase 3 studies and the requirements that would be needed to get the drug approved.
Q. Can you turn to page ending in Bates Number 8244. And this is -- on 8244, this is the section called "Dose Selection, 8.4"?
A. Yes.
Q. And then turning on to page 8245, the bottom paragraph, it says "Therefore, Biogen Idec believes that the 240-milligram TID BG0012 is the dosage with the most favorable benefit/risk profile, and subjects in the Phase 3 studies, when randomized to BG00012 active treatment, will receive 240-milligram TID."
Do you see that?
A. Yes.
Q. So here Biogen is representing to the FDA that it believes that 240-milligram TID dose, or 720 milligrams, has the most

favorable benefit/risk profile, correct?
A. That's what it says, yes.
Q. Why would Biogen choose to test a dose that did not have the most favorable benefit/risk profile?
A. Obviously, the 240-milligram TID dose had the most favorable benefit/risk profile because it had been shown to be safe and effective in Phase 2. We also know that 360 milligrams, or 120 milligrams TID, was also safe in Phase 2 but not statistically significant from an efficacy perspective.

Therefore, we thought it would be important to test 240 milligrams BID in the Phase 3. And the reasons for that were that Gilmore strongly believed the 240 milligrams BID was an important dose to test. We had enough safety data at the 720-milligram dose and at the 360-milligram dose to be confident that 240 milligrams BID would be safe in MS patients in Phase 3.

And MS is a chronic disease. It's very hard to take a TID dosing schedule over the long haul in any chronic disease. And since 720 milligrams was effective, we thought it would be important to test the 480-milligram dose -- i.e., 240 milligrams BID -- in the Phase 3s.

And, by the way, it's not uncommon to go into Phase 3 with a dose that you have not actually tested in Phase 2. That is not uncommon. As long as you have straddled that dose in Phase 2 from a safety perspective and you have, you know, a

dose that's effective, you can test a lower dose. In addition to the one that's proven to be safe and effective in Phase 2, you can test the slightly lower dose in Phase 3. And that happens not uncommonly in drug development.

Q. But there's nothing in this dose selection section that indicates at all that Biogen was considering testing the 480-milligram dose, correct?

A. No. We did not share that with the FDA for the reasons that I explained earlier.

Q. I would like to mark as Exhibit 18 a document Bates-labeled BiogenF10032834 to 32840.

A. I've reviewed the document.

Q. Have you seen this document before?

A. Yes.

Q. And what is it?

A. This is the meeting minutes compiled by the FDA regarding the end of Phase 2 meeting on BG-12 in MS held on August 30th, 2006.

Q. And would these minutes be kept in the ordinary course of Biogen's business?

A. Yes.

Q. And looking at the page ending in Bates Number 836, under the list of Biogen Idec attendees, you're listed there second from the bottom; is that correct?

A. Yes.

Q. On the next sentence says "The sponsor's questions are presented below in italics, followed by the preliminary FDA response conveyed to the sponsor by email just prior to the meeting and then a summary of the discussion from the meeting."

Do you see that?

A. Yes.

Q. And then turning to the page ending in Bates Number 2838.

A. Yes.

Q. At the bottom there, there's that Question 3C, which states "Is the selection of dose appropriate for the Phase 3 studies?" And then in brackets "Section 8.4."

Do you see that?

A. Yes.

Q. So that's in italics. Those are the questions that Biogen presented to the FDA?

A. Yes.

Q. But in terms of the dose of BG-12 administered, it was 720 milligrams per day, correct?

A. Yes, that's correct.

Q. So in response to Biogen's question of whether the selection of dose is appropriate for the Phase 3 studies, the FDA states "We agree that tolerability issues appear to limit the maximum dose to be tested to 240 milligrams TID. You should, however, consider testing intermediate doses in the Phase 3 study, e.g., 240 milligrams BID or 120 milligrams TID.

Such a dose might improve patient compliance and/or minimize dropouts from adverse effects during the study."

Do you see that?

A. Yes.

Q. So in response to Biogen's questions regarding its dose selection, the FDA stated that Biogen should consider testing an intermediate dose, such as 240 milligrams BID, correct?

A. The FDA said that we should consider testing intermediate doses in the Phase 3 study, for example, e.g., 240 milligrams BID or 120 milligrams TID. They did not require us to test intermediate doses below 720 milligrams in the Phase 3 studies.

Q. Is this the contingency that Biogen was planning for?

A. Yes. The team was preparing for potential feedback from the FDA regarding the dose.

Q. And then, if you look a couple paragraphs down, it says "Meeting Discussion."

A. Yes.

Q. And there it states "Biogen Idec indicated that the 240-milligram TID group has shown continued efficacy and proposed that dose as the best choice."

Do you see that?

A. Yes.

Q. So in response to the FDA's comment about testing an intermediate dose, Biogen maintained that the 720-milligram-per-day dose was the best choice; is that

correct?
A. We continued to say that we would include the 240-milligram TID dose in Phase 3. That was the dose that was shown to be safe and effective in the Phase 2 study. And there really wasn't any reason to debate with the FDA whether or not we'd include a lower dose in the Phase 3 studies. We had many other topics that we needed to talk about with them.
Q. So then Biogen only discussed its plan to test the 240-milligram TID dose, correct?
A. We did not say that that's our only choice here. We said it's the best choice, but we don't say it's the only choice of dose.
Q. Right. But that was the only dose that Biogen discussed that it would be testing with the FDA?
A. We proposed, yes, the 240-milligram PO TID as the dose to be tested in Phase 3.
Q. And no other dose amounts were discussed in response to the FDA's comments about testing an intermediate dose?
A. No, we did not discuss with them in detail which doses should be tested in the Phase 3 study, you know, other than the 720-milligram dose.
Q. So at the meeting Biogen didn't tell the FDA that it, in fact, did plan to test an intermediate dose of 480 milligrams per day?
A. No, we did not say that in the meeting.

Q. So if Biogen had been concerned, as we previously discussed, about the FDA's response to its planned dose of 720 milligrams per day, why wouldn't it also discuss the 480 milligram dose when the FDA itself brought it up?
A. There's no reason to because, if you have the FDA's agreement regarding your top dose and they think that's an appropriate dose to test in Phase 3, then you already know that you can test lower doses after that.
Q. Right. So you have their approval for the top dose. But what if the FDA states to you that you should consider an intermediate dose? Wouldn't that be a time to say we are testing that dose?
A. No. No, because they did not require it. They did not require it. They simply asked us to consider. And we know that, if we have their agreement for the 720-milligram dose, we could include a lower dose and, of course, we would get their agreement on that subsequently when they reviewed the protocols, the final versions of them.
Q. So what about that study, in your view, was the diligent pursuit of a 480-milligram dosing form of BG-12?
A. Because we had two doses that, you know, straddled the 480-milligram dose. We had the 720-milligram dose as the high dose, and then we had the 360-milligram dose. That provided us with the opportunity, if 720-milligram was safe and effective, to take on the 480-milligram BID -- sorry -- 240-milligram BID

dose subsequently in Phase 3.

Q. So, specifically, what about the Phase 2 study or its results meant that Biogen was diligently pursuing 480? I heard you say that it provided an opportunity to test it, but what did it teach Biogen about 480?

A. Well, it taught us that 720-milligram was safe and effective. It also shows that 360-milligram was safe. And, therefore, it gave us the opportunity to test a dose in between those two doses in the Phase 3 study.

Q. Okay. So, in your view, it was the opportunity to test a dose in between that meant that Biogen was diligently pursuing 480. Am I understanding?

A. Not the opportunity. The date that you got from the Phase 2 study enabled you to subsequently test 240-milligram BID in Phase 3.

Q. So, in your view, doing the Phase 2 study and seeing its results and data provided Biogen data to study 480?

A. Yes, it did.

And, by the way, that's not unprecedented. So there are other programs where you test a certain range of doses in Phase 2 -- bless you -- and then in Phase 3 you actually take doses that are in between those doses. So there are examples of that in drug development.

Q. So, in your view, did the Phase 2 trial teach Biogen that 480 was likely to be an effective dose of BG-12?

A. It did not tell us whether or not it was going to be effective. That still needed to be tested in Phase 3. But it did give us information that it would be safe.

Q. You said it did not tell us whether it would be effective, but did it suggest that it was likely to be effective?

A. We didn't really know that until we actually tested it in Phase 3. We didn't know if it was going to be effective.

MS. BLOODWORTH: That concludes the testimony, Your Honor.

THE COURT: All right. Thank you very much.

And I think that concludes our trial day. We'll begin tomorrow morning. You tell me whether you want to start at 8:30, 9:00, based on what you know your day is going to include. I'm sure it's Friday and some of you are anxious to be gone. So I would assume an earlier start is what you're focused on. But if not --

MS. BLOODWORTH: Thank you, Your Honor. I think --

MR. MONROE: I think, based on the representations, regarding hour and a half --

MS. BLOODWORTH: I think if we start at 9:00, we should be good, Your Honor.

THE COURT: All right. So, everybody, we will adjourn and resume at 9:00 tomorrow morning here. Thank you.

Court stands adjourned until 9:00 tomorrow morning.

(Proceedings concluded at 5:11 p.m.)

CERTIFICATE

I, Cindy L. Knecht, Registered Professional Reporter and Official Reporter of the United States District Court for the Northern District of West Virginia, do hereby certify that the foregoing is a true and correct transcript of the proceedings had in the above-styled action on February 6, 2020, as reported by me in stenotypy.

I certify that the transcript fees and format comply with those prescribed by the Court and the Judicial Conference of the United States.

Given under my hand this 6th day of February 2020.

/s/Cindy L. Knecht

_____

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Official reporter, United States
District Court for the Northern
District of West Virginia